AN ANALYSIS OF POST SURGICAL OUTCOME IN PRIMARY VESICO URETERIC REFLUX PATIENTS

Dissertation submitted to

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the regulations
for the award of the degree of

M.Ch BRANCH-V

PEDIATRIC SURGERY

2009-2012

MADRAS MEDICAL COLLEGE
CHENNAI-3

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY
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INSTITUTIONAL ETHICS COMMITTEE
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CERTIFICATE OF APPROVAL

To
Dr. A.E. Poornima
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Madras Medical College, Chennai -3.

Dear Dr. A.E. Poornima

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the propoal entitled "An analysis of Post surgical outcomes in primary Vesico Uretric Reflux Patients" No. 23062011.

The following members of Ethics Committee were present in the meeting held on 24.06.2011 conducted at Madras Medical College, Chennai -3.

1.	Prof. S.K. Rajan, MD	-- Chairperson
2.	Prof. V. Kanagasabai MD Dean, Madras Medical College, Chennai-3,	-- Deputy Chairman
3.	Prof. A. Sundaram, MD Vice Principal , Madras Medical College, Chennai -3	-- Member Secretary
4.	Prof R. Sathianathan MD	-- Member
5.	Prof R. Nandhini, MD Director, Institute of Pharmacology, MMC, Ch-3	-- Member
6.	Prof. Geetha Subramanian MD DM Prof & Head , Dept. of Cardiology, MMC, Ch-3	-- Member
7.	Prof. Pregna B. Dolia MD Director , Institute of Biochemistry, MMC, Ch-3	-- Member
8.	Prof. C. Rajendiran .MD Director , Institute of Internal Medicine, MMC, Ch-3	-- Member
9.	Thiru. A. Ulaganathan Administrative Officer, MMC, Chennai -3	-- Layperson
10.	Thiru. S. Govindasamy . BA.BL	-- Lawyer
11.	Tmt. Arnold Soulina	-- Social Scientist

We approve the proposal to be conducted in its presented form

Sd /. Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report

Member Secretary, Ethics Committee

CERTIFICATE

This is to certify that the dissertation entitled **"AN ANALYSIS OF POST SURGICAL OUTCOME IN PRIMARY VESICO URETERIC REFLUX PATIENTS"** is a bonafide work done by **Dr.A.E.POORNIMA** under our guidance's and supervision during the period between 2009 - 2012 towards the partial fulfillment of requirement for the award of M.Ch Branch V (Paediatric Surgery) degree examination held in August 2012 by The Tarmlnadu -Dr. M.G.R. Medical University, Chennai.

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DECLARATION

I solemnly declare that the dissertation entitled "**AN ANALYSIS OF POST SURGICAL OUTCOME IN PRIMARY VESICO URETERIC REFLUX PATIENTS**" is the original work done by me at the Institute of Child Health & Hospital for Children, Egmore during the M.Ch Course (2009-2012), under the guidance and supervision of Prof.S.V.Senthilnathan M.S., M.Ch., Professor and H.O.D. of Paediatric Surgery. The dissertation is submitted to The Tamil Nadu Dr.M.G.R. Medical University towards the partial fulfillment of the regulations for the award of M.Ch (Branch – V) in Paediatric Surgery.

Place: Chennai
Date: 12.03.2012

Dr. A.E. POORNIMA

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INTRODUCTION

Vesico ureteral reflux is a dynamic event – the retrograde flow of bladder urine into the upper urinary tracts. It's a feature of disordered anatomy and function at the uretero vesical junction.

Although this reflux nephropathy may disappear during growth, it is of clinical concern because of the morbidity from ascending urinary infection and associated nephropathy that can lead to hypertension and renal function insufficiency.

To reduce the morbidity and mortality associated with vesico ureteric reflux, there are many studies available all over the world with relation to the pre-op work up, medical and surgical management, post operative follow up and outcome.

So, we have undertaken this study on "An analysis of post surgical outcome in primary vesico ureteric reflux (VUR) patients" at Institute of Child Health, Madras Medical College, Chennai-8.

AIMS AND OBJECTIVES OF THE STUDY

The aim of the study is

- To analyse the post surgical outcome in primary vesico-ureteral reflux patients with the clinical and imaging parameters in the follow up.
- To analyse the primary vesico ureteral reflux treated surgically with those treated by chemoprophylaxis alone.

REVIEW OF LITERATURE

The ureters are bilateral tubular structures responsible for transporting urine from the renal pelvis to the bladder. They are generally 22 to 30 cm in length.

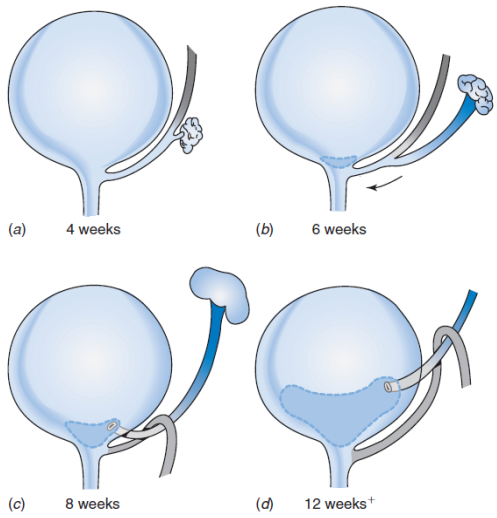
During the 4th week of gestation, the development of the ureter begins as an outpouching of the mesonephric duct, termed the ureteric bud. The development of this structure is heavily influenced by molecular factors released from the mesodermal tissue mass, which is destined to become the renal parenchyma (i.e. the metanephric blastema)[1]. At 28 days, the ureter consists of an epithelial tube surrounded by loose mesenchymal cells. Transient luminal obstruction ensues, with subsequent recanalization during the 7th week of gestation. It appears that this recanalization process begins in the midureter and extends in a bidirectional manner both cranially and caudally. It has been suggested that angiotensin exerts its effect through angiotensin 2 receptor (AT2) and may play a role in this recanalization process. Chwalle's membrane, a two-layered cell structure, transiently divides the early ureteric bud from the urogenital sinus. Subsequent dissolution of this membrane results in unimpeded flow of urine from the kidney into the bladder.

The first signs of ureteral muscularization[2] are seen at 12 weeks of gestation. Smooth muscle differentiation is first noted at the ureterovesical junction (UVJ) and then ascends cranially towards the upper collecting

system. With time, these fibers, which are initially randomly arranged in the wall of the ureter, become more numerous and assume a more specific orientation. The epithelium attains a transitional configuration by 14 weeks. Once fully developed, the muscular wall of the ureter is characterized as having an inner longitudinal, middle circular, and outer longitudinal layer. As the ureter penetrates the bladder, its muscular layers disperse. The outer layer melts into the detrusor in the upper part of the hiatus to form Waldeyer's sheath, which attaches the ureter to the bladder and is in continuity with the deep trigone. As the ureter makes its transition to an intramural location, the muscle fibres take on a primarily longitudinal orientation. The longitudinal muscle fibers spread out to form the borders of the superficial trigone.

Proper development and spatial orientation of the ureter as it combines with the bladder are dependent on a number of molecular factors. The renin-angiotensin system[3] appears to play a major role in ureteral development. Angiotensin 2 is expressed in high concentration by the mesenchymal cells that are positioned adjacent to the ureteric bud at an early developmental stage. The fact that expression of this receptor markedly decreases after birth supports the contention that angiotensin 2 might play an important role in ureteral development. Mice in whom the angiotensin 2 gene has been knocked-out demonstrate a high incidence of congenital anomalies of the urinary tract, including VUR, UVJ obstruction, and megaureter. These structural anomalies may result from delayed apoptosis of the mesenchymal cells surrounding the ureteric bud.

The clinical relevance of these experimental findings has been underscored by the identification of a select group of patients with mutations at this locus who possess a syndrome that includes ureteropelvic junction (UPJ) obstruction and megaureter. Proper spatial orientation of the ureter is probably dependent on genes responsible for cell specification and body segmentation. The PAX family of genes has been extensively studied in this regard. These genes appear to play a role in the interplay between the ureter and the developing kidney. PAX mutations have been implicated in syndromes with VUR and renal anomalies and are inherited in an autosomal dominant manner. However, to date, neither mutations in the PAX genes nor in other genes involving body segmentation have been demonstrated to any significant degree in patients with familial VUR.



Embryology of ureter and trigone. The ureteral bud develops into the ureter and induces the metanephric blastema to differentiate and become the kidney. The common excretory duct (segment of mesonephric duct caudal to the ureteric bud) is absorbed into the bladder and becomes the deep trigone.

Vesico Ureteral Reflux (VUR) is a dynamic event – the retrograde flow of bladder urine into the upper urinary tracts. Though it occurs normally in the young of many animal species, it is considered abnormal in humans. It is a feature of disordered anatomy and function at the ureterovesical junction (UVJ). In practice, VUR describes a common primary disorder of childhood associated with urinary infection and renal scarring, or reflux nephropathy. Although the reflux event usually disappears during growth, the disorder is of clinical concern because of the morbidity from ascending urinary infection and the associated nephropathy that can lead to hypertension and renal function insufficiency.

Many studies have been directed at isolating the causal relationships between the pathophysiologic components of the VUR disorder, the reflux event, the urinary infection and the associated nephropathy. The VUR disorder in overall is a heterogenous condition with diverse features, suggesting that compound factors may operate in the genesis of the reflux and its relationships with urinary infection and nephropathy.

Most studies are concerned with older children with acquired renal scarring. Most children presenting in clinical practice do so after urinary infection and already have renal scarring.

VUR – the Anomaly:

VUR was first documented in 1893, when Pozzi noted the reflux of urine from the distal segment of a ureter accidentally severed during pelvic surgery.Prevalance is 1-2%.

When prenatal USG is used for screening, foctus with a prenatal renal pelvis dilatation is greater than or equal to 4mm, identified VUR is 6.9%, with an incidence of 0.44% of the population screened by prenatal USG. In infants investigated after an established and specific diagnosis of prenatal hydronephrosis, the incidence increases to 15% to 25%, i.e. a prevalence rate of 0.02% to 0.2%. Prenatal screening identifies only a few of all children who present with VUR at some stage.

Investigations after clinical presentation with urinary infection show reflux present in 30%-50%. Boys present predominantly in the first year of life often with severely dilated upper urinary tracts and often congenital nephropathy. Girls present cumulatively throughout childhood and have less upper tract dilatation. By the age of 2 years, girls presenting with VUR slightly exceeds boys and thereafter girls predominate.

VUR may have a genetic basis, as there is an incidence of 32% among siblings (100% for identitical twins and if a parent is affected, the risk increases to 69%). No specific gene has been identified yet.

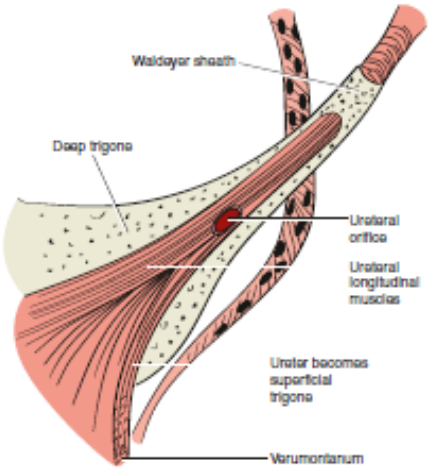
Ureterovesical Junction:

The UVJ is structurally and functionally adapted to allow the intermittent passage of ureteral urine and to prevent the reflux of bladder urine. For this the ureter enters the bladder with an oblique intramural passage which extends submucosally to open onto the trigone.

Reflux is prevented by active and passive components, the natural tonus of the ureteral muscles maintains an active closure of the intravesical ureter except during the efflux of urine. The longitudinal urethral muscles intermingle with those of the (superficial) trigone and the contralateral ureter so that contraction elongates the submucosal tunnel. The adventitia fuses with a fibrous sheath (Waldeyer)[4]. Circumferentially allowing the intramural ureter to move within the hiatus during bladder filling. As the bladder fills and becomes distended, there is progressive obliquity of the intravesical ureter, the trigone is progressively stretched, increasing resistance in the intravesical ureter and causing increased pressure within the distal end of the ureter.

During micturition, when the trigone is stimulated, the intravesical ureter is pulled downward and the ureteral walls are compressed against the supporting vesical wall as a passive reinforcement of the valvular mechanism. These actions anchor the ureter, retaining its correct configuration and preventing lateral displacement of the ureteral orifice. The mechanism requires a complex of muscular components that includes ureteral and vesical muscle bundles and an elaborate neural influence.

Neurohistochemistry has defined a dual autonomic innervation by cholinergic and nor adrenergic nerves, and these is evidence for neuropeptides that may act as neuromodulators.



The classical view of the ureterovesical junction. The ureter enters the bladder with an oblique passage to open onto the trigone. There is a seamless continuity between the ureter and the trigone, which extends in males to the verumontanum. The adventitia fuses with Waldeyer sheath. The longitudinal ureteral muscles extend and fuse with the uscles of the opposite ureter to form the superficial trigone.

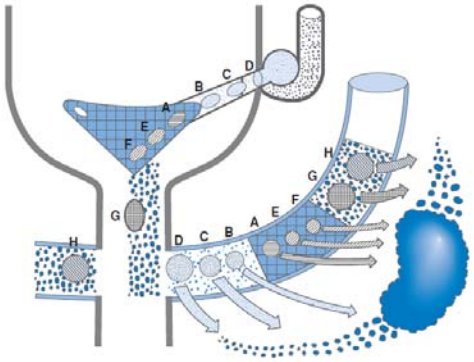
Immunohistochemistry has revealed further abundant innervation at the UVJ and numerous nitric oxide synthase immuno reactive nerves that may have a regulatory role, as evidenced from separate biochemical and functional studies.

Genesis of VUR:

The well accepted explanation is immaturity affecting the length of the submucosal tunnel[5] in younger children and its spontaneous resolution during growth. The intravesical ureter (the intramural segment and the submucosal tunnel) lengthen from 0.5cm in neonates to 1.3 cm in adults, the mature length is achieved by 10-12 years of age.

Factors:

- Short intravesical ureter
- Trigonal and distal ureteral muscle deficiency.
- Reduced nerve supply
- Disordered extracellular matrix.
- Ureteral muscle atrophy and dysplasia at VUJ.



The position of the ureteral bud on the wolffian (mesonephric) duct corresponds to the final position of the ureteral orifice and differentiation of the metanephric blastema. Lateral and caudal ectopia can both result in renal dysplasia (Meckie and Stephans).

Induction and Orientation of the ureteral bud & renal development:

Primary VUR is an abnormal UVJ with maldevelopment, malfunction or delayed maturity. Secondary VUR is associated with outflow obstruction.

In terms of the low pressure / high pressure reflux – the worse renal prognosis is often seen in the low pressure group in which reflux occurs freely from early in the filling phase through golf hole orifices into highly abnormal kidneys.

Whereas high pressure reflux was a secondary effect occurring at high pressures either late in filling or in voiding when bladder function was abnormal and finally overcome the resistance at the VUJ.

Spontaneous resolution documented by contrast study by the international Reflux study reported a 28% resolution rate after 5 years and 47% after 10 years. For older population with grades III & IV reflux-in boys faster resolution occurs than in girls. Sustained squirt of high pressure, infected urine reflux into a nonciliated ureter may present the greatest potential for acquired renal scarring.

PATHOPHYSIOLOGY OF VUR:

1) Immature Bladder:

Incomplete detrusor/sphincter synchrony[6] during voiding results in an interrupted urinary flow with intermittent high bladder pressures as the detrusor contracts against a closed or only partially relaxed sphincter. Immature voiding dynamics and recurrent UTI significantly delay the resolution of infantile VUR. It is more probable that the functional abnormality lies in an individual's susceptibility to urinary infection, which then effects changes to bladder, ureteral and trigonal function with resultant reflux.

2. *Urinary Infection:*

Infection distorts bladder function and may be the factor in initiating many cases of dysfunctional elimination syndromes, whereas others have no identifiable cause for bladder instability or detrusor overactivity.

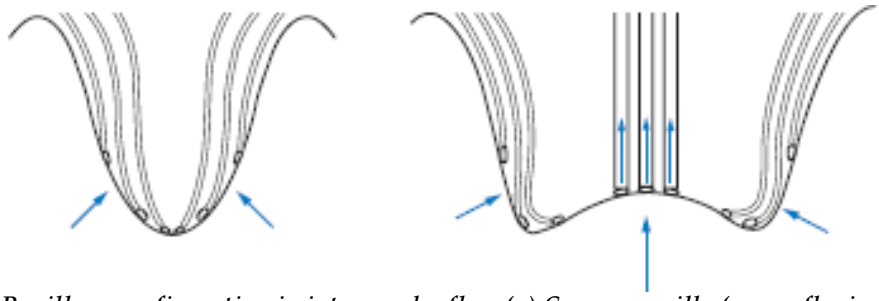
Reflux Associated Nephropathies:

The term was first used in 1973 – the congenital reflux nephropathy. It may arise through several mechanisms, affecting the developing kidney and manifests as a spectrum of abnormalities. Scars are seen as defects in Isotope uptake Tc 99m DMSA. The definitive macrosopic features of reflux nehropathy are coarse segmental scars, involving cortex and medulla, overlying dilated (or clubbed) calyces. Scar contracture with hypertrophy of the unaffected renal parenchyma can cause an uneven lobular appearance of the renal outline and renal poles are often more prominently affected. The changes are interstitial with chronic inflammatory cell infiltration[7] and lymphoid follicle formation together with tubular atrophy and interstial fibrosis. There is 14% incidence of new scars during the first 5 years of follow up and rare subsequently. Bilateral nephropathy is a high risk factor for chronic insufficiency and the development of hypertension.

Pathogenesis of acquired renal scarring-intra renal reflux:

Intra renal reflux has a segmental distribution occurring predominantly at the renal poles regions where scars are common.

There is a direct transmission of bladder pressure[8] to the renal pelvis and the intra renal back flow occurs as an extension of the reterograde dynamics. This exposes the renal tubules to pressures as that in bladder, so that urinary pathogens gain access to renal substance. The segmental distribution of intrarenal reflux is due to variation in renal papillary morphology. Two types of papillae, the compound papilla and simple papilla are present. Compound papillae present as flat or concave cribiform areas bearing open Belleni ducts allowing intrarenal reflux in poles of the kidney. Simple papillae present a convex surface with slit like orifices that create a valvular mechanism preventing intrarenal reflux and found in mid zone. Ransley and Risdun showed that scar formation in the presence of urinary infection occurred only in relation to refluxing papillae (i.e) bigbang nature of the acquired scars.



Papillary configuration in intrarenal reflux. (a) Convex papilla (non-refluxing): crescentric or slit-like orifices of collecting ducts opening obliquely onto the papilla. (b) Concave or flat papilla (refluxing papilla): round, gaping orifices of collecting ducts opening at right angles onto flat papilla.

Urinary Infection:

Experimental studies after urinary infection with UVR showed rapid progression from small direct abscesses reflecting individually affected

tubules to coalescent abscess or a confluent mass. Within two weeks irreversible scaring occurs and by three weeks scar contracture occurs.

The use of antimicrobial therapy in one week after infection or during early inflammatory phase will limit the extent of scar formation and any residual pathology presents as fine linear scars. Hence rapid treatment for acute pyelonephritis limits renal damage.

Acquired Pyelonephritis in the absence of VUR:

Presence of renal scarring in the absence of VUR is a feature of spontaneous resolution of VUR. Alternative explanations for the genesis of non-reflux pyelonephritis are

a) haematogenous spread of infection.

b) ascending pyelonephritis in the absence of reflux

c) transient VUR during an acute infection – ^{99m}Tc DMSA scintigraphy is highly sensitive in detecting the initial stages of pyelonephritis.

Sterile VUR and acquired renal scarring:

Sterile VUR in itself does not cause renal scars. In severe outlet obstruction as in PUV in infants, scarring sometimes involved numerous papillae owing to distortion of the papillary morphology and recuritment of previously non refluxing papillae. Scar formation resulted from tubular

interstitial damage with rapid progression to interstitial collagen deposition but without the cellular inflammatory response.

Pathogenic Mechanism of renal scarring:

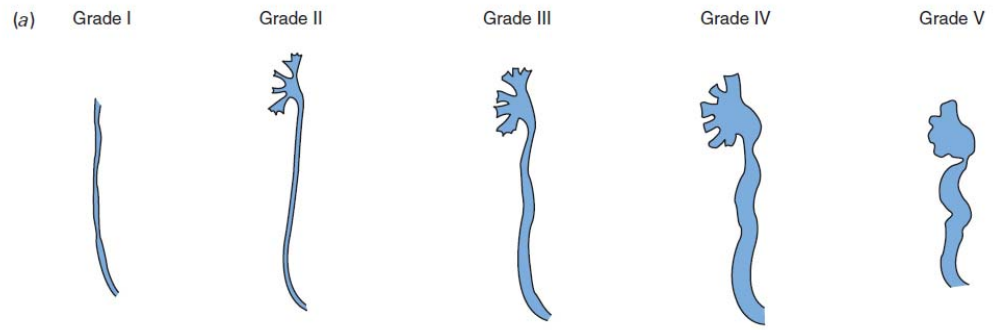
Fibrosis which constitute the scars, results from increased cell matrix synthesis and deposition together with a decrease in degradation mediators like cytokines, growth factors and angiotension II. Ischaemia and reperfusion damage the release of superoxide, and free radicals of oxygen destroys lipid cell membranes.

There is a transient elevation of renal vein renin during early inflammatory phase of pyelonephritis due to compression of vasa recta and peritubular capillaries by edema or from obstruction of the capillary vasculature with platelet and granulocyte aggregation. Reperfusion injury can be limited by use of exogenous superoxide dismutase, complement depletion, pretreatment with the xanthine oxidase inhibitor-allopurinol. In There are no adverse effects of VUR on renal growth[9,10] or glomeurlar function.

DIAGNOSIS OF PRIMARY VUR:

Voiding Cystourethrogram:

Retrograde imaging of bladder and urethra was first described in 1905. It's the principle method for assessing the reflux and classification by the International study group into five grades.



(a) International classification of vesicoureteral reflux: grade I, ureter only; grade II, ureter, pelvis, calices, no dilatation, normal caliceal fornices: grade III, mild or moderate dilatation and/or tortuosity of ureter, and mild or moderate dilatation of the pelvis, but no or slight blunting of the fornices; grade IV, moderate dilatation and/or tortuosity, of ureter and mild: dilatation of renal pelvis and calices, complete obliteration of sharp angle of fornices but maintenance of papillary impressions in majority of calices, grade V, gross dilatation and tortuosity of ureter, gross dilatation of renal pelvis and calices, papillary impressions are no longer visible in majority of calices. (Modified from International Reflux Committee

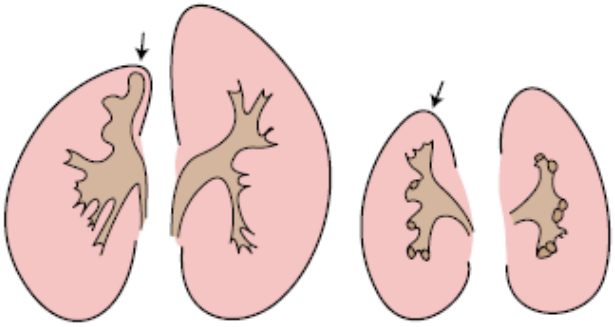
Common Classifications of Vesicoureteral Reflux:

Description	***Grade/Classification***					
International Study Classification	0	I	II	III	IV	V
Dwoskin-Perlmutter	0	1	2a	2b	3	4
Birmingham	0	1	2	←	3	→
Australia/NZ		←	Mild →	Moderate	←	Severe →
Great Britain		I	II (Voiding)	III (filling & voiding)		IV (Dilatation)

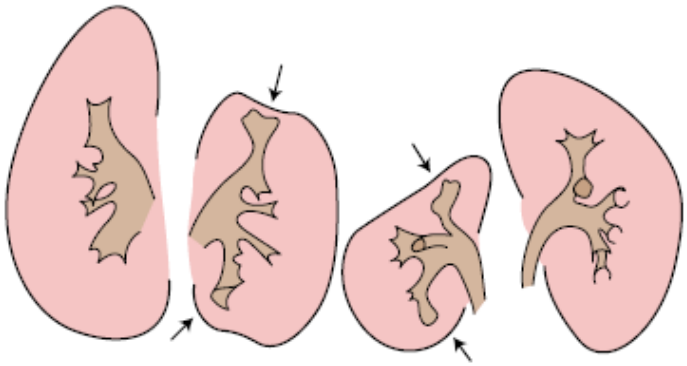
International study classification has been used in our study.

Radionuclide Studies:

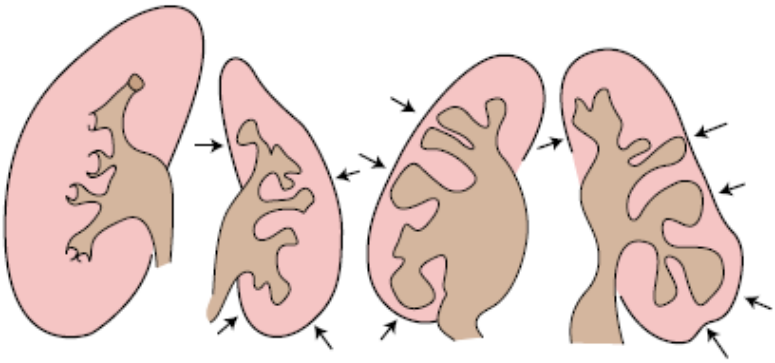
Renal scanning using ^{99m}Tc DMSA is the preferred method of assessing growth and development of kidneys.



1. Upper pole scarring



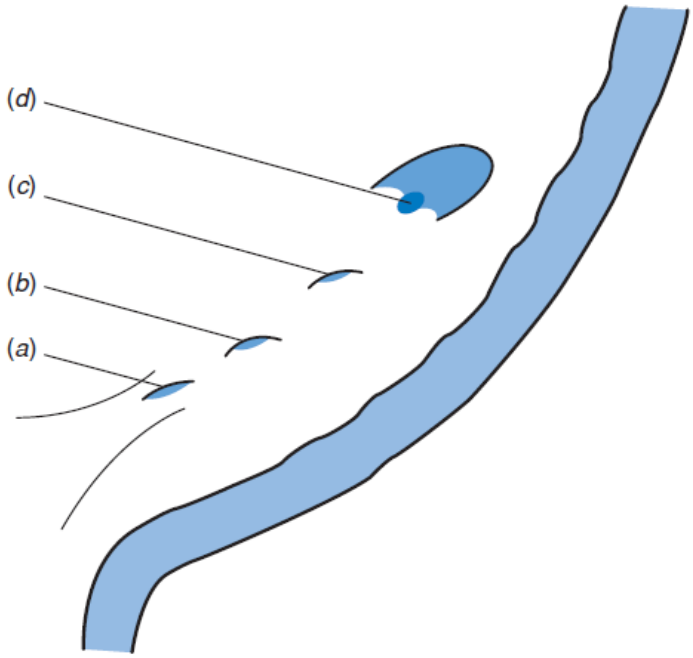
2. Upper and lower pole scarring



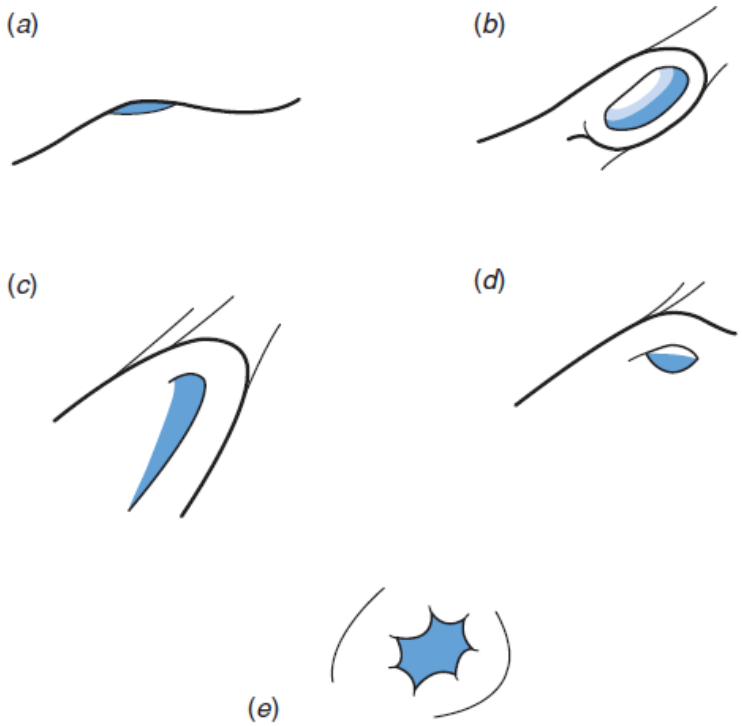
3. Generalized scarring

Common areas of renal scarring characterized by parenchymal thinning over a deformed calyx, as determined from intravenous pyelograms. The extent of scarring may be related to single polar scars; multiple areas of upper, lower, and medial scars; or generalized scarring, as depicted

Ultrasonography studies the upper and lower tract. ***Colour Doppler USG*** images the directional flow of urine[11].



Four different ureteric orifice positions: (a) normal; (b) moderately lateral; (c) very lateral; and (d) orifice at the mouth of a diverticulum



Orifice morphology (endoscopic view): (a) normal cone-shaped orifice; (b) stadium orifice; (c) horseshoe orifice; (d) lateral pillar defect; and (e) golfhole orifice. (Reproduced from Glassberg et al).

Other diagnostic modalities.

1. Magnetic resonance voiding cystography.

2. PIC cystography – positioning the instillation of contrast – the contrast instilled at the orifices will unmask the occult VUR.

Non Imaging Modalities[12]

Measured levels of microproteinuria, urine retinol binding protein, urinary prostaglandin F2, urinary B2–microglobulin, TammHorsfall protein, B-N-Acetyl Hexosaminidase, Nacetyl D-Glucosaminidase (NAG) Urinary interleukin levels, procalcitonin, serum endothelium leukocyte adhesion molecule–1 (ELAM-1) are elevated.

Who should be tested for reflux:[13]

- All UTI in 1st year of life in male child.
- Rec. UTI in female child.
- One episode of pyelonephritis has 9% incidence of scarring where as three attacks had 38% of patients with renal scars.
- No new scars developed after puberty.
- Youngest children are at greatest risk for renal scarring from bacterial pyelonephritis due to low intra renal reflux pressure, immature immune system and delayed recognition of pyelonephritis or inadequate treatment.

Identical twins have been observed to have reflux by autosomal dominant inheritance and Asian and African ancestry have lower incidence of reflux. In neonates with antenatal hydronephrosis, 38% had reflux even though post natal USG was normal.

Condition associated with Primary VUR:

- Renal Agenesis
- Horshoe kidney and renal ectopia
- Mutli cystic dysplastic kidney .
- Prune belly syndrome.
- Mega cystis – megaureter syndrome.
- Hypospadias.
- Duplication, Ureterocele, ectopic ureter
- Imperforate anus.

MANAGEMENT OF VUR:

1) Medical Management
2) Endoscropic Management
3) Surgical Management

1) MEDICAL MANAGEMENT:

Treating each infection after it was diagnosed was unsafe as, though not all children developed scars, it was impossible to predict who will be affected. Renal damage on IVP can occur even after one infection.

Data from the international reflux study in children showed a high rate of new scar formation in children not on continuous prophylaxis.

In Goldraich and Goldraich's study there was a 3% rate of new scar formation in those on chemoprophylaxis, unilateral reflux (54%) resolved slightly more than the bilateral (12%) cases in the international reflux study in children. Resolution rates were grade I – 83% Grade II – 60%, Grade III – 46%, Grade IV – 9% and grade V – 0%.The mean age of resolution was 4.6 years and mean time of resolution was 1.7 years.

According to Birmingham (United kingdom) Co-operative study: Those on chemoprophylaxis – their urine cultures were obtained once in every 3 months for 2 years and then once in every 6 months. Renal function was studied at 2 and 5 years with creatinin clearance and water deprivation tests.

The indications for surgery were,

1) Break through infection.
2) High reflux grade in adolescence.
3) New renal scars.
4) Progressive renal insufficiency.
5) Poor compliance.
6) UTI after antibiotics were stopped.

The rate of break through infection was 25%. In the international reflux study group there were no new cases of hypertension and GFR was not reduced, renal growth was same between the medical and surgical

group. The number of new scars or deterioration in renal function was equal in surgical and medical groups. There was more febrile UTIs in medically managed patients. Most of new scars in surgical group were within 1 year of surgery[14]. Meta-analysis by Wheeler and colleagues showed that overall risk of febrile and non febrile GTI occurring in either group was the same after 5 years.

ANTIBIOTIC PROPHYLAXIS:

Characteristics of commonly used urosuppressive antibiotics

Drug	***Therapeutic Dose***	***Suppressive Dose***	***How Supplied***	***Comments***
Nitrofurantoin	2 mg/kg PO qid	1 mg/kg PO qid	Suspension (5mg/mt) Capsule (25,50mg)	Avoid in patients <1 month of age. Not effective if CrCl <40 ml/min. Nausea common with suspension; Sprinkling macrocystals may avoid this
Trimethoprim sulfamethoxazole	4 mg/kg trimethoprim +20 mg/kg sulfamethoxazole PO bid	2 mg/kg trimethoprim +10 mg/kg sulfamethoxazole PO qd	Suspension (8 mg trimethoprim +40 mg sulfamethoxazole per ML. Tablet (80mg trimethoprim, 400mg sulfamethoxazole)	Avoid in patients <1 month of age contraindicated with hyperbilirubinemia. May cause blood dyscrasias and Stevens- Johnson syndrome.
Trimethoprim (Primsol)	5 mg/kg PO bid	2 mg PO qd	Oral solution 50mg/5ml	Avoid in patients <2 months of age.
Amoxicillin	10mg/kg PO tid	10mg/kg PO qd	Suspension (25,50 mg/ml) Drops 50/mg/ml)	Avoid in patients <2 months of age.
Cephalexin	25 mg/kg PO bid	25 mg/kg qd	Suspension 125 mg/5ml or 250 mg/5ml.	Alternative for neonates

Indications for Urinary Tract Prophylaxis:

- Vesicoureteral reflux
- Recurrent infections with normal urinary tract

- Awaiting radiological evaluation after urinary tract infection.
- Unstable urinary tract abnormality (e.g. partial urinary tract obstruction)
- Urethral instrumentation
- Immunosuppression or immunocompromise.
- Infants with first urinary tract infection before 8-12 wk of age.

Patient compliance was varying from 12-90% with higher compliance with high grade reflux. Breakthrough infection is defined as the development of an infection with an organism resistant to prophylaxis, breakthrough infections are more common if there is voiding dysfunction. Scarring occurs mostly after febrile infections. There is no consensus on the number of break through infections that can be safely tolerated before recommending surgery. Scott reported a 29% rate of cystitis after spontaneous resolution. The Birmingham study found that most new scars occurred between ages of 2 and 7 years, but scars could progress at any age.

Macharen and Simpson correlated high renal scar rates with reflux occurring at low bladder volumes.

Micromolecular and genetic predictors of scarring are presence of

1) DD genotype of the angiotension converting enzyme gene.
    1) Tumour necrosis factor α AA genotype
    2) Tissue Kallikrein promoters
    3) Transforming growth factor B1

4) Insulin like growth factor-1 MRNA expression

5) Interleukin 6 & Interleukin -8

6) Cyctooxygenase 2 over expression

7) Urinary endothelin -1

There are no large, long term prospective studies to establish safe guidelines for discontinuing prophylaxis based on grade, sex, race, renal scarring or voiding habits.

Spontaneous resolution rates:

Study by Edward and Coworkers revealed spontaneous cessation in 85% of children whose ureters are not dilated and in 40% of children whose ureters are dilated.

Kaplan meier curves predict time course for resolution of reflux[15] as 50% with grade I within 2.5 years, Gr.II with 5 years of diagnosis and Gr.III & IV within 8 years of diagnosis.

Spontaneous resolution in special anatomic situations:

1) Complete Ureteral Duplication

High grade lower pole reflux with ureteral dilatation and lower pole atrophy have a low resolution rate and needs early surgical correction.

2) Periureteral bladder diverticulum:

Large diverticulum with ureter entering directly into it have less chance of resolving, than a smaller diverticulum.

3) Solitary Kidney:

Low grade reflux followed medically whereas high grade reflux are treated as those for two kidneys.

4) Intra renal reflux:

Presence of intra renal reflux is an absolute indication[16] of the abandonment of a continuous prophylactic regimen.

5) In antenatally diagnosed dilatation of foetal renal pelvis – post natal incidence of VUR even in normal post natal USG is high with break through infection in 1st 3 months.

6) Voiding habits and voiding dysfunction:Double or triple voiding will help eliminate bacteria that had returned to the bladder from the upper tracts after an episode of reflux during the first void. More incidence of breakthrough infection in voiding dysfunction.

7) Circumcision reduces the incidence of recurrent infection in boys younger than 1 year.

8) Risk of renal failure is less than 1% - 0.5% proteinuria is the hall mark of progressive segmental glomerulosclerosis. Hypertension develops during adolescence when there is extensive renal scarring which account for 14-50 of cases.

9) Glomerular disease does not recur in the transplanted kidney even if it is also refluxing.

10) Renal failure can be accelerated by pregnancy in women with pre-existing renal insufficiency and chemoprophylaxis during pregnancy or anti reflux surgery before pregnancy is recommended.

2) ENDOSCOPIC TREATMENT:

Tissue augmenting substances for endoscopic subureteral injection.

1) Dextroromer/Hyaluronic acid copolymer
2) Poly tetra fluro ethylene.
3) Cross linked bovine collagen.
4) Polydimethylosiloxane.
5) Autologus chondrocytes.
6) Calcium hydroxyl apatite.

Indications for endoscopic correction of VUR are the same as for open anti reflux operations via the cystoscope subureteral injection of Deflux is given until a bulge appears in the floor of the submucosal ureter.

Results of subureteric Teflon injection (STING) is complete resolution after 1 injection in 76%, after 2 injections in 12% and after 3-4 injection in 2%, while symptoms improved in 6% and failed results in 4% of cases.

3) SURGICAL MANAGEMENT FOR VUR:

Absolute indication for surgical correction failures of medical management[17]. Specifically break through febrile UTIs.

Relative indications include massive reflux (Grade IV & V) associated congenital abnormalities of VUR, secondary reflux.

Bacteriuria has been reported in 40% of patients after successful surgery, although most do not develop pyelonephritis. Renal growth retardation or the presence of new renal scars dilating reflux persisting in girls who have reached full somatic growth potential. Hutch first reported the successful correction of VUR in 1952. The Goal of surgical correction is the restoration of the flap valve mechanism.

History:

The first reported ureteroneocystostomy was by Tanffer in 1877. Later Bovee described 80 cases of ureteral reimplant. In 1952, Hutch reported the successful correction of VUR by a combined extra vesical and intra vesical dissection.

Many surgical techniques have been described Politano and Lead better described intravesical mobilization of the terminal ureter with subsequent reimplantation through a new vesical hiatus and submucosal tunnel. Paquin's requirements for a successful VUR surgery include a tension free ureteral anastamosis and a submucosal tunnel length five times longer than the diameter of the ureter.

Extravesical approach was described by Lich. Gregoir & Van Regemorter simultaneously. Glenn and Anderson used modified ureteral advancement technique without creating a new muscular hiatus in 1960's.

Cohen then modified the ureteral advancement procedure – achieved adequate submucosal tunnel length by using posterior aspect of the bladder for cross trigonal tunneling.

Cystoscopy is performed prior to reimplantation surgery to evaluate the lower urinary tract.

Surgical Techniques:

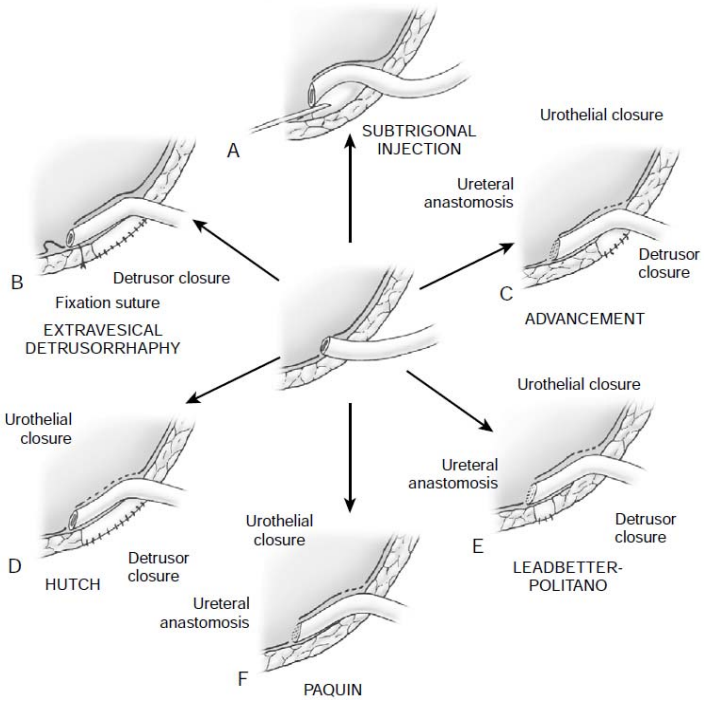
Intra Vesical Techniques:

Child is placed in supine position. Pfannenstiel skin incision is made and the anterior rectus sheath is opened in a horizontal fashion with superior and inferior rectus flaps. By extra peritoneal approach, the bladder is opened longitudinally after taking stay sutures. Moist sponges are placed in the dome of bladder and Denis brown retractor is used for exposure and to flatten the posterior bladder wall. This elevates the lower half of the bladder bringing the ureteral orifices into the middle of the operative field. Ureters are intubated with 3 or 5 Fr feeding tubes and mobilized with caution to avoid devascularisation.

a) Politano-lead better Technique:

The original politano-lead better technique was described in 1958. Ureter is mobilised, posterior bladder wall dissection is performed under vision and freed from peritoneum. A right angle clamp is passed through the original hiatus in a superior direction and hugging the posterior wall and marking the new site for entrance of ureter. The new hiatus location is

slightly medial and cephalad 2-3 cm above the original hiatus. Avoid excessive kinking of ureter and the original muscular opening is closed. Ureter enters through a new hiatus and a submucosal tunnel inferomedially towards the bladder neck. Ureter is fixed all around. A modification of politano – lead better original method is increasing the submucosal tunnel length.



Conceptual comparison of techniques to correct reflux. A common theme is the achievement of a long length of intravesicalureter based on a strong detrusor floor and covered with compressible urothelium.

b) Cohen's cross trigonal repair:

First described by Cohen in 1975. After ureteral mobilization, a submucosal tunnel is created along the posterior bladder wall without transferring the ureter to a new muscular hiatus. The major disadvantage of this procedure is the difficult intubation of the ureteral orifices after

surgery related to their transtrigonal location. New mucosal hiatus is created above the contralateral ureteral orifice. In bilateral reimplant the other ureter is brought to the new orifice close to the inferior portion of the old contralateral ureteral orifice.

c) Glens – Anderson Repair:

In 1967 Glenn Anderson popularized this technique which is used for laterally displaced ureters and a sufficient posterior bladder wall mucosal tunnel directed caudally and ureteral orifice is placed superior to the bladder neck.

d) Gil Vernet Repair:

Described in 1984, for those with lateral ectopia and widened mega-trigone. Advancing the mobile ureters across the trigone by using traction sutures placed at medial aspect of ureteral orifices. Mattress sutures advance the ureters towards the midline increasing their intramural length.

Extravesical Techniques:

a) Lich-Gregoir Repair:

This approach was described simultaneously by Lich-Gregoir and Van Regemorter in 1960. In this bladder is not opened, cystoscopy is performed to rule out any bladder abnormalities.

Bladder is partly filled. Ureters are exposed at its entrance in the posterior bladder wall and mobilized. The serosal and muscular layers of the detrusor are incised superiorly for a distance of 4-5cm to create a trough for ureter. The bulging bladder mucosa is seen. The ureter is advanced and anchored and placed in the trough. The detrusor is closed over it. Perivesical drain are not routinely used.

Specific Advantages and Disadvantages of commonly performed antireflux procedures

Procedure	Advantages	Disadvantages
Subtrigonal injection	Endoscopic procedure	Material injected: Teflon: migration, granuloma formation Collagen: uncertain durability
Extravesical detrusorrhaphy	Bladder never opened No hematuria No ureteral anastomosis Minimal bladder spasms Endoscopically accessible ureteral orifices	
Advancement Cohen (transtrigonal) Glenn-Anderson	Avoids complications of neohiatus formation as in Leadbetter-Politano reimplantation	Transtrigonal: difficult to access ureter endoscopically Glenn-Anderson: limited length of tunnel achievable
Hutch	No ureteral anastomosis Good alternative with large associated congenital diverticulum	
Leadbetter-Politano	Excellent ureteral tunnel dimensions with endoscopically accessible ureteral orifices	Risk of ureteral obstruction Risk of sigmoid colon injury with left reimplantation
Paquin	Versatility, extremely useful during complex reconstructive procedures	

POST-OPERATIVE EVALUATION:

Surgical repair of VUR via a catheterless uretero neocystostomy reduces hospital stay without increasing complication rates. Post surgical management includes renal USG at one month to assess the presence of hydronephrosis.

Chemoprophylaxis is continued for 3-6 months following surgery. Yearly follow up of voiding history, BP, urine analysis and renal USG are done.

A success rate for surgical method is 94-99%. The American Urological Association (AUA) Paediatric Vesicoureteral Reflux guidelines panel found an overall success rate of 95.6%. Reimplanted ureters with grade I-IV UVR – had a surgical correction rates of 98-99% regardless of the technique. Grade V VUR have been found to have a persistant lower grade VUR in 19% of cases following surgery.

SURGICAL COMPLICATIONS:

Ureteral Obstruction:

Mild hydrorephrosis may occur in early post operative period which resolved over a period of several months. Persistant hydronephrosis is related to ureteral obstruction. Initial management is by placement of percutaneous nephrostomy tube or indwelling stent. If obstruction persists, a repeat reimplant is required. A psoashitch or Boariflap, transuretero ureterostmy or ileal ureter may be received for reconstruction for given ureter length.

Persistent reflux:

Success rate is more than 98%. Adequate submucosal tunnel and ureteral tapering in dilated ureters are needed. In most cases reflux is downgraded and resolve with growth and good voiding habits. One

unusual cause of persistent VUR is the development of a ureterovesical fistula following reimplant surgery and needs surgical correction.

New Contralateral Reflux:

Following unilateral ureteric implant, new contralateral VUR occurs in 1-18%. Possible factors are prior history of resolved contralateral reflux, correction of Grade-V VUR and VUR into a duplicated system. It usually resolves in 1-2 years with good voiding regimen and rarely surgery is needed.

The open surgical repair for the correction of VUR is both a safe and effective management option. Politano-leadbetter and Cohens' cross trigonal methods are successful and used widely. Though laparoscopic and endourologic techniques are being performed in greater numbers, the ease and success of the open surgical repair is the standard by which all other repairs should continue to be judged.

1. The open surgical correction of vesico ureteral reglux is highly effective, has few complications, and is the current gold standard treatment.

2. The appropriate intravesical surgical technique is determined by trigonal anatomy.

3. The modified politano-leadbetter repair involves the creation of a new suprahiatal location of the ureter under direct vision.

4. When creating a new suprahiatal location for the ureter during the modified politano-lead better repair it is important to avoid lateral placement to prevent J looking of the ureter.

5. The cross trigonal method of ureteral reimplantation results in less potential for kinking because of its use of the original muscular hiatus.

6. The major drawback to the cross trigonal method is the subsequent difficult intubation of the ureteral orifice due to its position following surgery.

7. The Glenn-Anderson technique is highly successful when used in those patients with laterally displaced ureters, allowing for sufficient ureteral advancement and tunnel length.

Treatment recommendations: Boys & Girls with primary vesicoureteral reflux and with renal scarring

Clinical Presentation		Treatment					
		Initial (Antibiotic Prophylaxis or Open Surgical Repair)		Follow-up (Continued Antibiotic Prophylaxis, Cystography, or Open Surgical Repair*)			
Reflux Grade/ Laterality	*Patient Age (yr)*	*Guideline*	*Preferred Option*	*Reasonable Alternative*	*Guideline*	*Preferred Option*	*No Consensus†*
I-II/unilateral or bilateral	<1	Antibiotic prophylaxis					Boys and girls
	1-5	Antibiotic prophylaxis					Boys and girls
	6-10	Antibiotic prophylaxis					Boys and girls
III-IV/unilateral	<1	Antibiotic prophylaxis			Girls: surgery if persistent	Boys: surgery if persistent	
	1-5	Antibiotic prophylaxis			Girls: surgery if persistent	Boys: surgery if persistent	
	6-10		Antibiotic prophylaxis		Surgery if persistent		
III-IV/bilateral	<1	Antibiotic prophylaxis			Surgery if persistent		
	1-5		Antibiotic prophylaxis	Surgery	Surgery if persistent		
	6-10	Surgery					
V/unilateral or bilateral	<1		Antibiotic prophylaxis	Surgery	Surgery if persistent		
	1-5	Bilateral: surgery	Unilateral: surgery			Surgery if persistent	
	6-10	Surgery					

Treatment recommendations: Boys and Girls with Primary Vesicoureteral Reflux and No Renal Scarring

Clinical Presentation		Treatment					
		Initial (Antibiotic Prophylaxis or Open Surgical Repair)		Follow-up (Continued Antibiotic Prophylaxis, Cystography, or Open Surgical Repair*)			
Reflux Grade/ Laterality	*Patient Age (yr)*	*Guideline*	*Preferred Option*	*Reasonable Alternative*	*Guideline*	*Preferred Option*	*No Consensus†*
I-II/unilateral or bilateral	<1	Antibiotic prophylaxis					Boys and girls
	1-5	Antibiotic prophylaxis					Boys and girls
	6-10	Antibiotic prophylaxis					Boys and girls
III-IV/ unilateral or bilateral	<1	Antibiotic prophylaxis			Bilateral: surgery if persistent	Unilateral: surgery if persistent	
	1-5	Unilateral: antibiotic prophylaxis	Bilateral: antibiotic prophylaxis				
	6-10		Unilateral: antibiotic prophylaxis	Bilateral: antibiotic prophylaxis		Surgery if persistent	
			Bilateral: surgery			Surgery if persistent	
V/unilateral or bilateral	<1		Antibiotic prophylaxis		Surgery if persistent		
	1-5		Bilateral: surgery	Bilateral: antibiotic prophylaxis	Surgery if persistent		
			Unilateral: antibiotic prophylaxis	Unilateral: surgery			
	6-10	Surgery					

According to the 1977 AUA guide lines, Medical treatment is preferred to surgery in early infancy because of a higher rate of spontaneous resolution. However its also been shown that the incidence of pyelonephritis was twice as high in patients treated with antibiotic prophylaxis than those treated surgically and once pyelonephritis occurs infants are more susceptible to renal scarring than older children.

The success of medical line of therapy can be judged on the basis of the following:

a) Reflux resolution – lower grade reflux has a better chance of resolving.

b) Renal scarring – many studies show no statistical difference in rate of new scarring treated medically or surgically. The Birmingham reflux study identified new scars after 5 years in 6% of medically treated and 5.2% of surgically treated patients.

c) Renal growth and function – No evidence to show that renal growth is impaired in unscarred kidneys exposed to sterile reflux of any grade. Though surgical correction stabilizes the GFR it does not lead to long term improvement.

d) Urinary tract infection – in children with grade II-IV VUR the incidence of pyelonephritis is higher in medically treated than in those who underwent surgical therapy.

So comprehensive medical therapy involves good bladder training and continuous antibiotic prophylaxis.

Cases in which there is parenteral anxiety regarding long term effects of antibiotic prophylaxis in infants and children and x-ray exposure for repeated VUG as well as psychological trauma due to urethral catherisation and in some groups such as those with uncontrollable UTI, urosepsis or non compliance of medical treatment, surgical treatment may be reasonable to avoid further renal damage and may be socially indicated.

MATERIALS AND METHODS

This a prospective study conducted in the department of pediatric surgery, Institute of Child health over a period of 2½ years.

This study was performed between August 2009 and January 2012 for primary vesico ureteral reflux.

Apart from the clinical examination, baseline investigation, blood parameters, ultrasonogram – voiding cystourethrogram intravenous urogram and DMSA scan were taken.

Patients were followed up for and more year post operatively for resolution of reflux and urinary tract infection.

Patients treated surgically were compared with those treated with chemoprophylaxis alone in terms of recurrent urinary tract infections and resolution of reflux as demonstrated by voiding cystourethrogram.

SELECTION CRITERIA:

Inclusion Criteria:

All patients with primary vesico ureter reflux (i.e due to intrinsic defect within the ureterovesical junction) irrespective of grade or laterality.

Exclusion Criteria:

All patients with secondary vesico ureteral reflux as a result of another pathology like associated bladder outlet obstruction (posterior urethral valve) and neurogenic bladder dysfunction are excluded from the study.

OBSERVATION

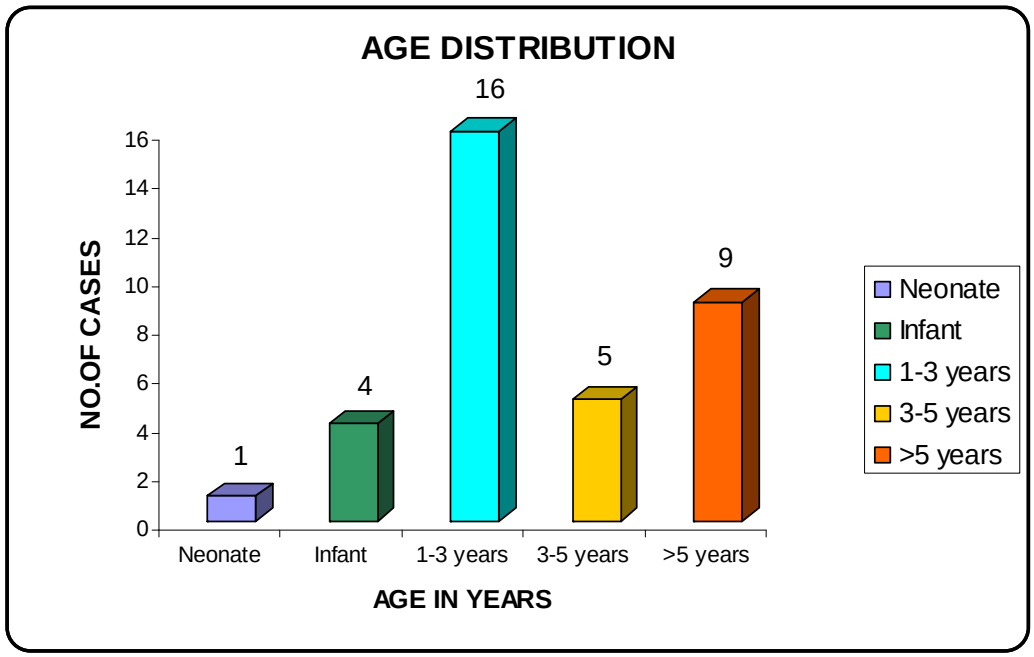
This is a prospective study conducted in department of pediatric surgery ICH and HC over a period of 2½ years August 2009 – January 2012.

The following facts were obtained. During this study period 35 patients who met the selection criteria attended the paediatric surgery department.

Age Distribution in Numbers:

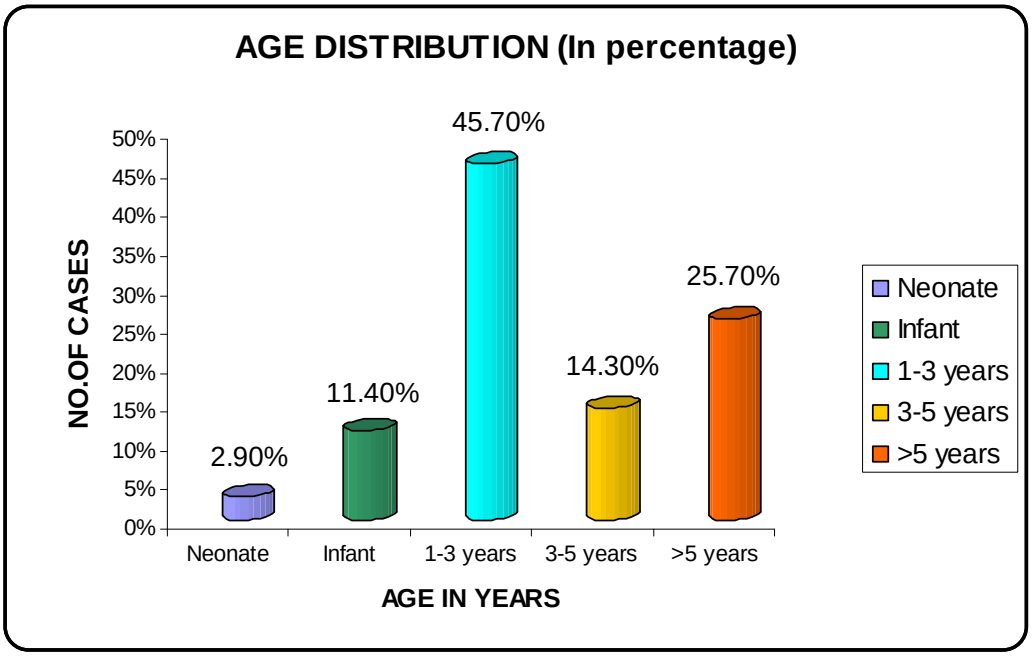
Age	***No. of cases***
Neonate	1
Infant	4
1-3 years	16
3-5 years	5
>5 years	9
Total	35

Range – neonate to 12 years.



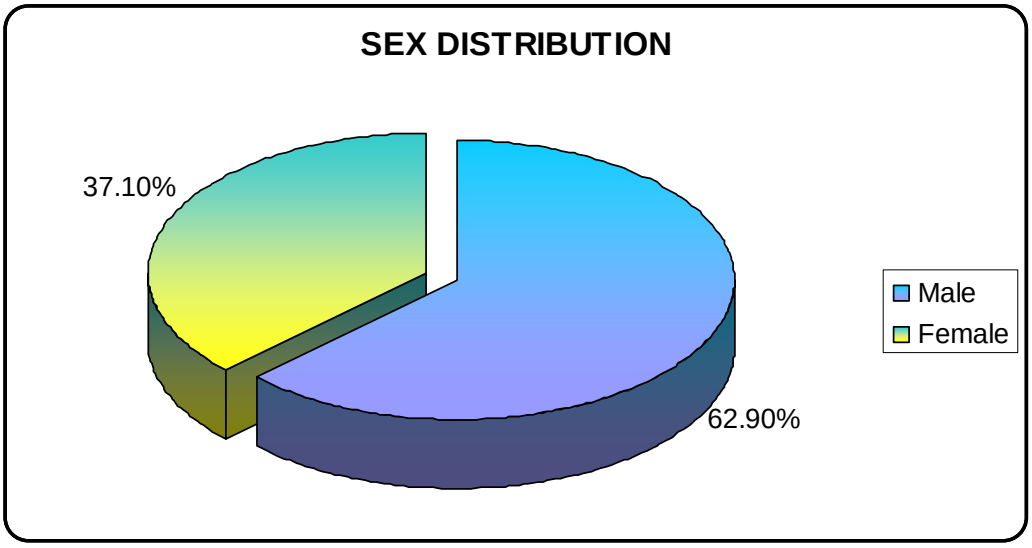
Age Distribution in Percentage:

Age	*% of cases*
Neonate	2.9%
Infant	11.4%
1-3 years	45.7%
3-5 years	14.3%
>5 years	25.7%
TOTAL	100%



Sex Distribution:

Sex	*No. of cases*	*Percentage*
Male	22	62.9%
Female	13	37.1%
Total	35	100%

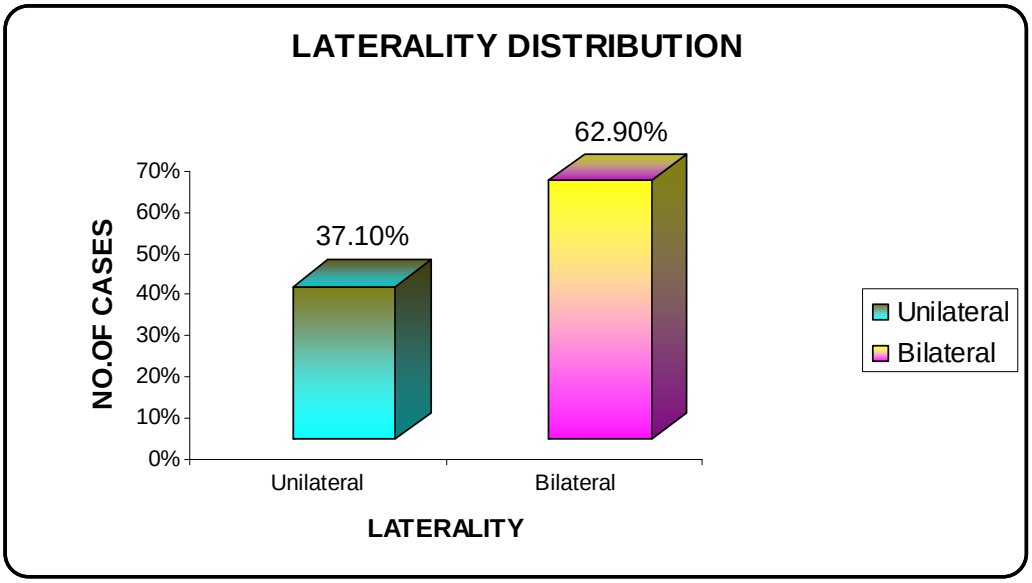


Laterality Distribution:

Laterality	*No. of cases*	*Percentage*
Unilateral (R) or left	13	37.7%
Bilateral	22	62.9%
TOTAL	35	100%

Ratio

Unilateral : Bilateral = 1: 1.7

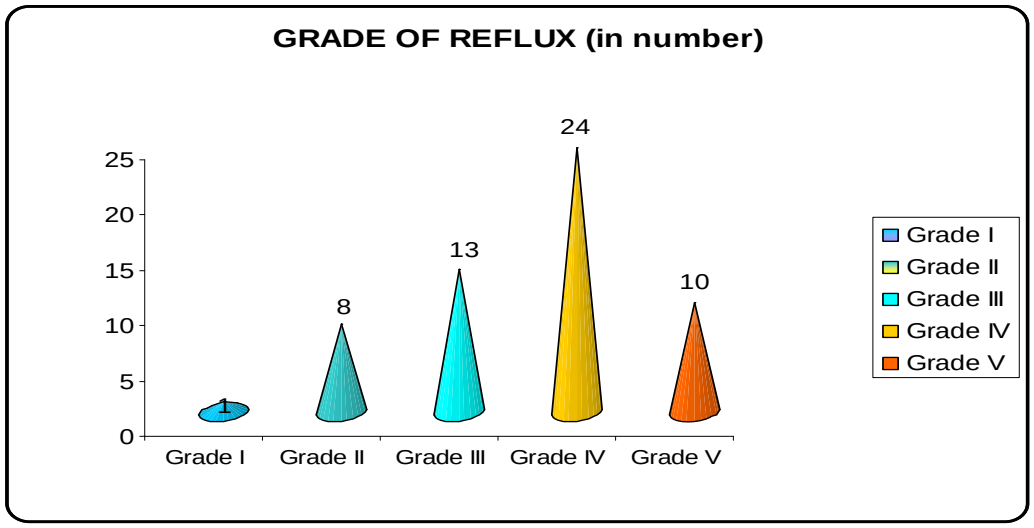


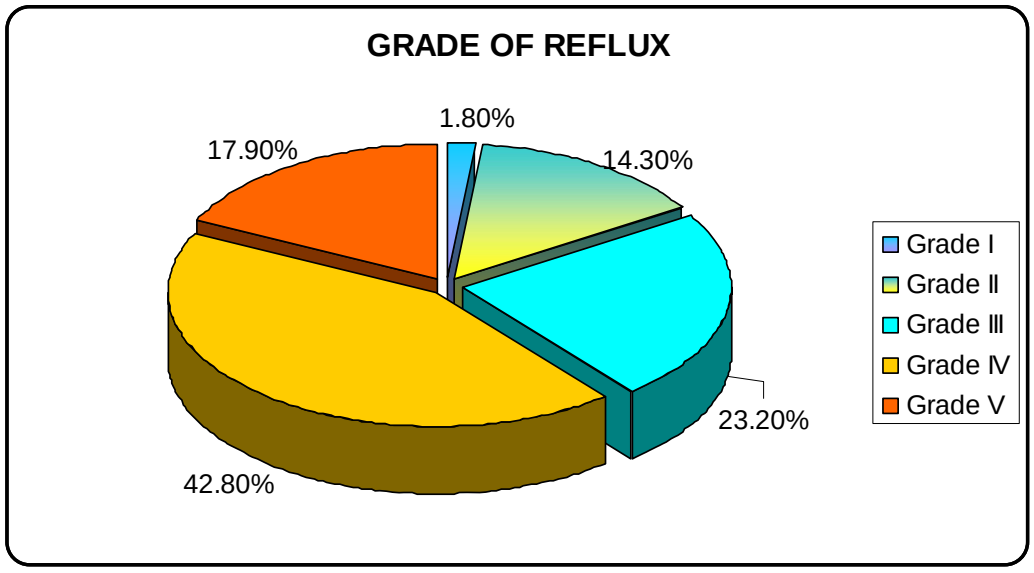
MCU SHOWING VARYING GRADES OF REFLUX

MCU SHOWING VARYING GRADES OF REFLUX

Grade of Reflux:

Grade of vesico ureteral reflux	***No. of Renal Units***	***Percentage***
Grade I	1	1.8%
Grade II	8	14.3%
Grade III	13	23.2%
Grade IV	24	42.8%
Grade V	10	17.9%
Total	56	100%





Hypertension:

Hypertension was present in 1 patient.

Urine Culture:

All patients had history of urinary tract infection with urine culture positive for E.coli.

Blood Urea and Creatinine:

Blood urea & creatinine were raised in	3 cases
Blood urea & creatinine were raised normal in	32 cases
Total	35 cases

Ultrasound:

In ultrasound examination an increase in diameter of the ureter and/or renal pelvis was observed as a sign of reflux.

Bilateral uretero hydronephrosis was detected in 3 cases antenately.

Associated findings in USG:

Contracted/small kidney size	- 4 cases
Double moiety	- 2 cases
Non visualized / absent kidney	- 1 case
MCDK	- 1 case

Antenately diagnosed bilateral ureterohydronephrosis – 3 cases

Presenting complaint:

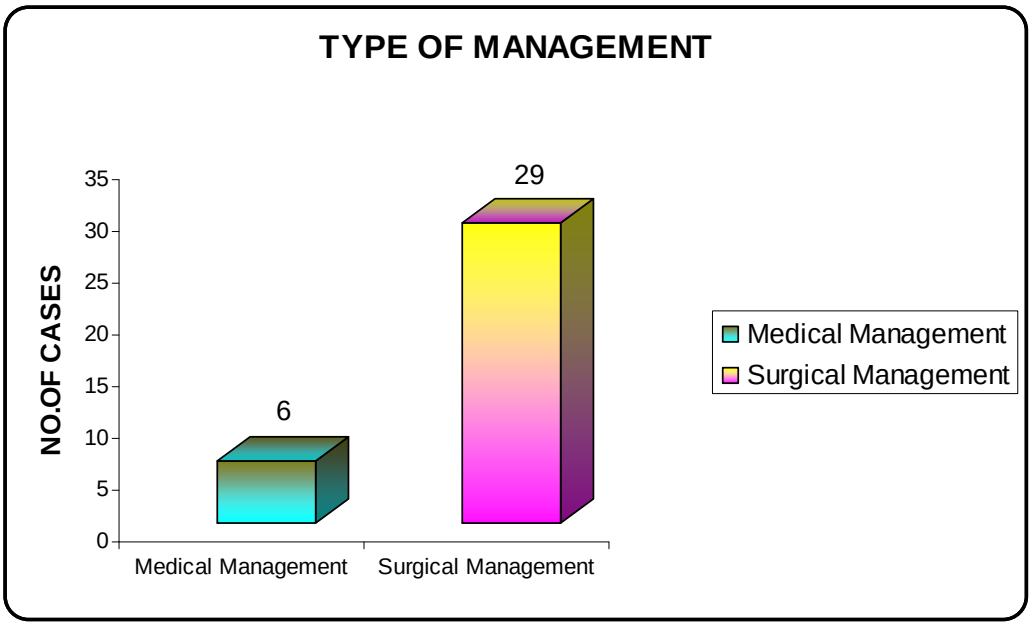
Recurrent urinary tract	- 32 cases
Asymptomatic	- 3 cases
Total	- 35 cases

All patients underwent voiding cystourethrogram (VCUG) and were graded according to the criteria of the international reflux study committee.

Micturating cystourethram was done in all patients preoperatively and on post operative follow up.

During the study period one case was lost for follow up while on medical management.

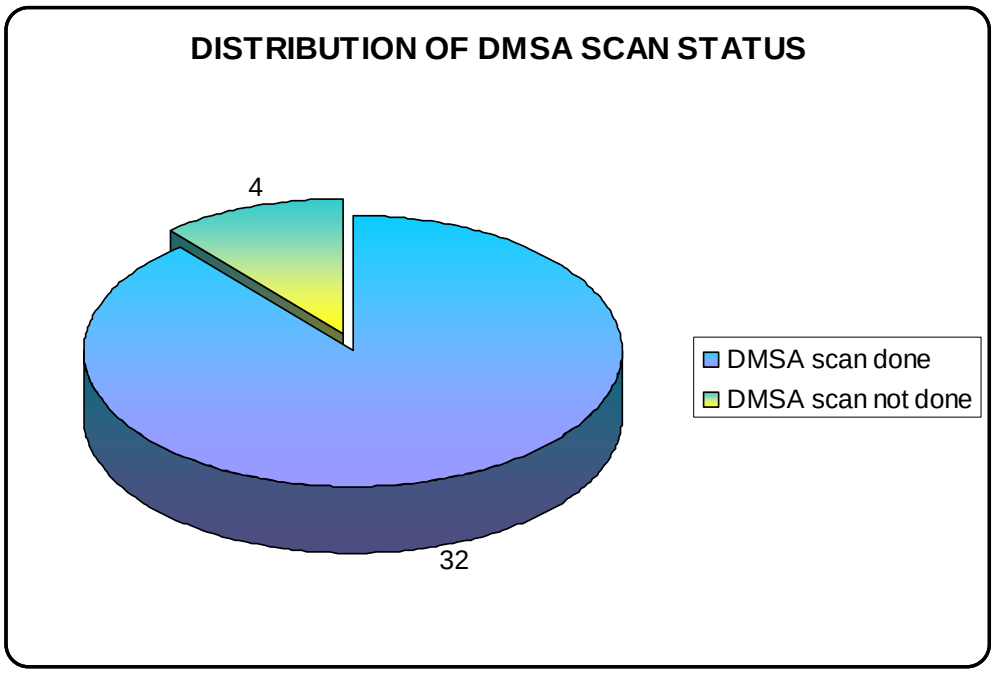
Medical Management	- 6 cases
Surgical Management	- 29 cases
TOTAL	- 35 cases



DMSA scan

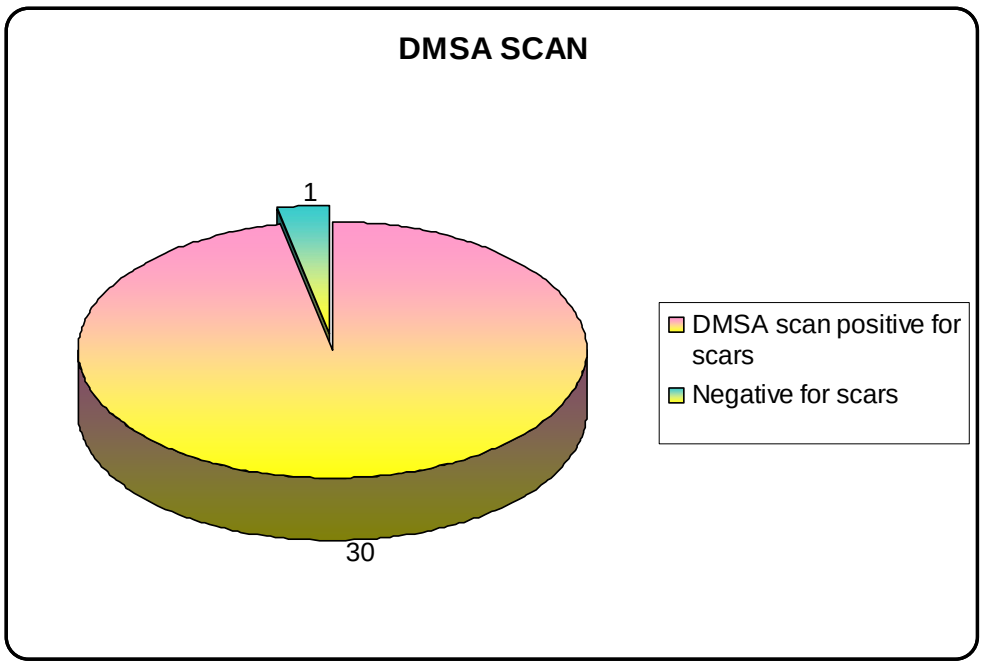
DMSA scan done	- 31 cases
DMSA Not done*	- 4 cases
Total	- 35 cases

* DMSA not done due to non affordability in 3 cases and loss of follow up in 1 case.



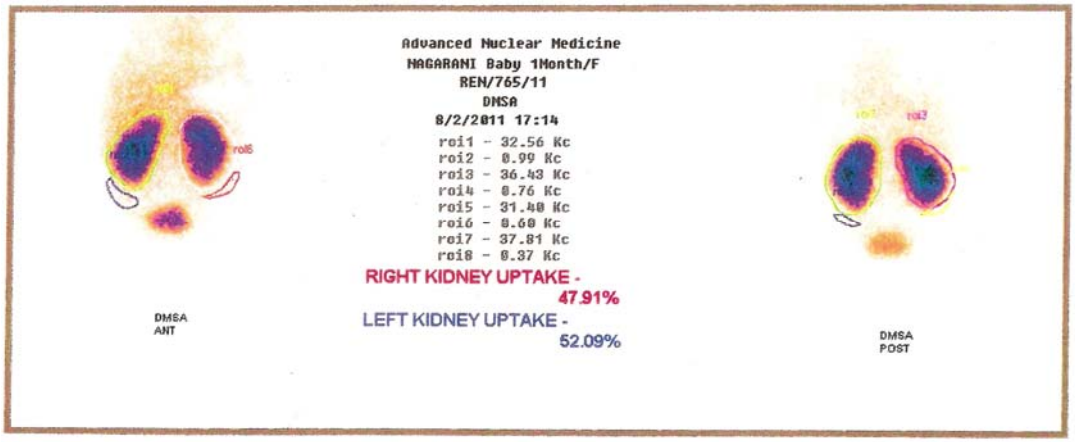
DMSA Scan

DMSA scan Positive for scars	- 30 cases
Negative for scars	- 1 case
Total	- 31 cases

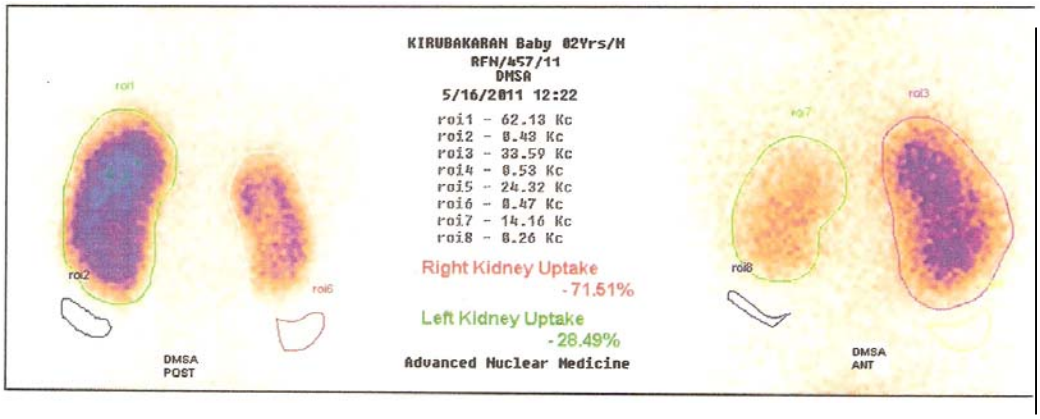


^{99M}TC DMSA RENAL SCINTIGRAPHY

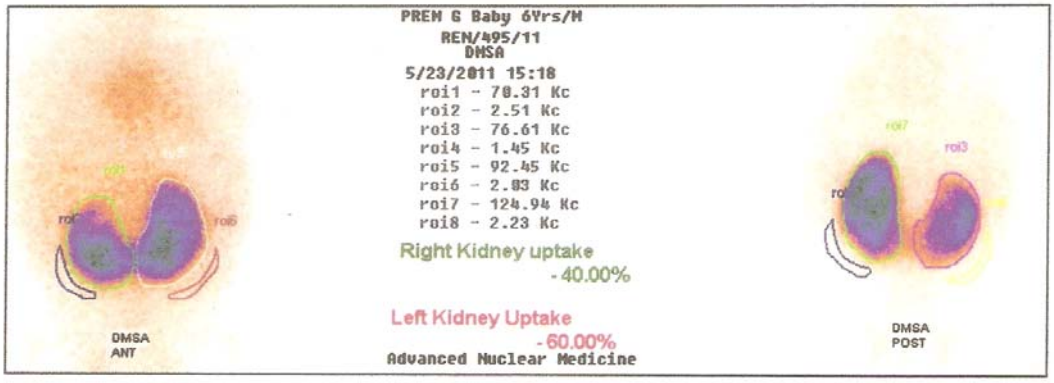
Study is negative for multiple renal scars in both kidneys



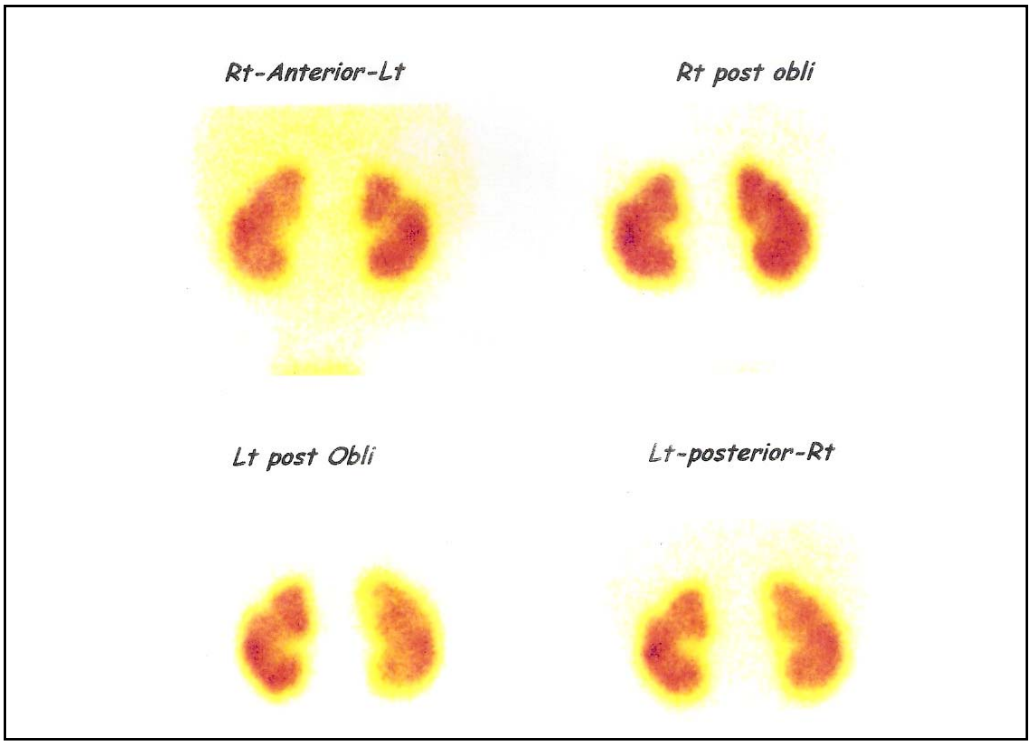
Study is Positive for multiple renal scars in both kidneys. There is relatively prominent involvement of the Left kidney



Horse shoe kidney with multiple renal scars in the upper pole of the less dominant Right kidney



Study is Positive for multiple renal scars in both kidneys.



CYSTOSCOPY:

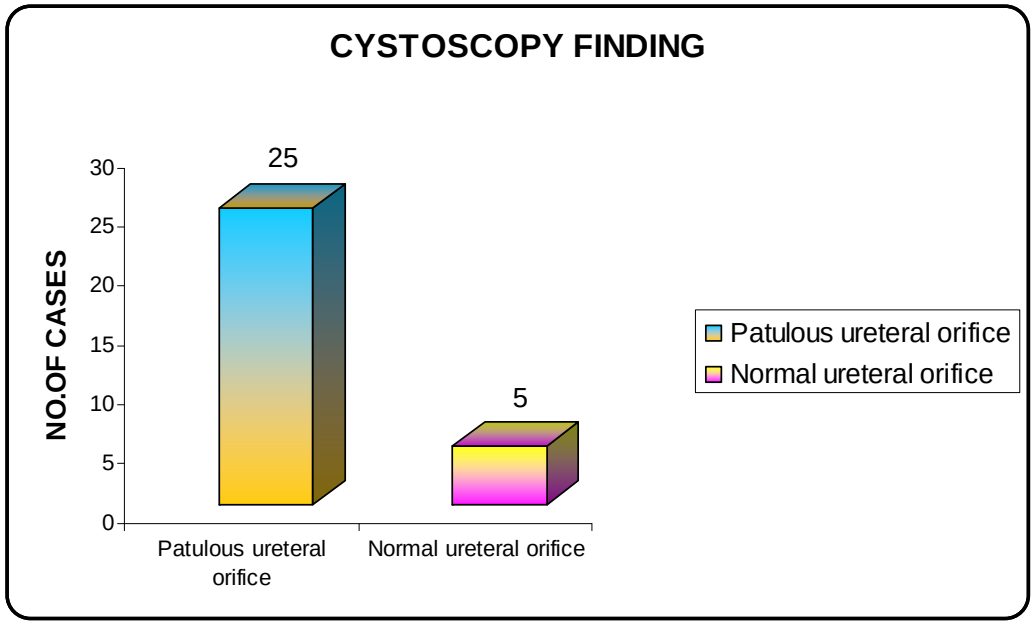
Cystoscopy done in 30 cases.

Findings:

Patulous ureteral orifice	25 cases
Normal ureteral orifice	5 cases

Cystoscopy not done in 5 cases.

Cystoscopy was not done as 4 patients were not willing for the cystoscope and 1 patient lost follow up.



TYPES OF SURGERY:

Cohens Reimplant:

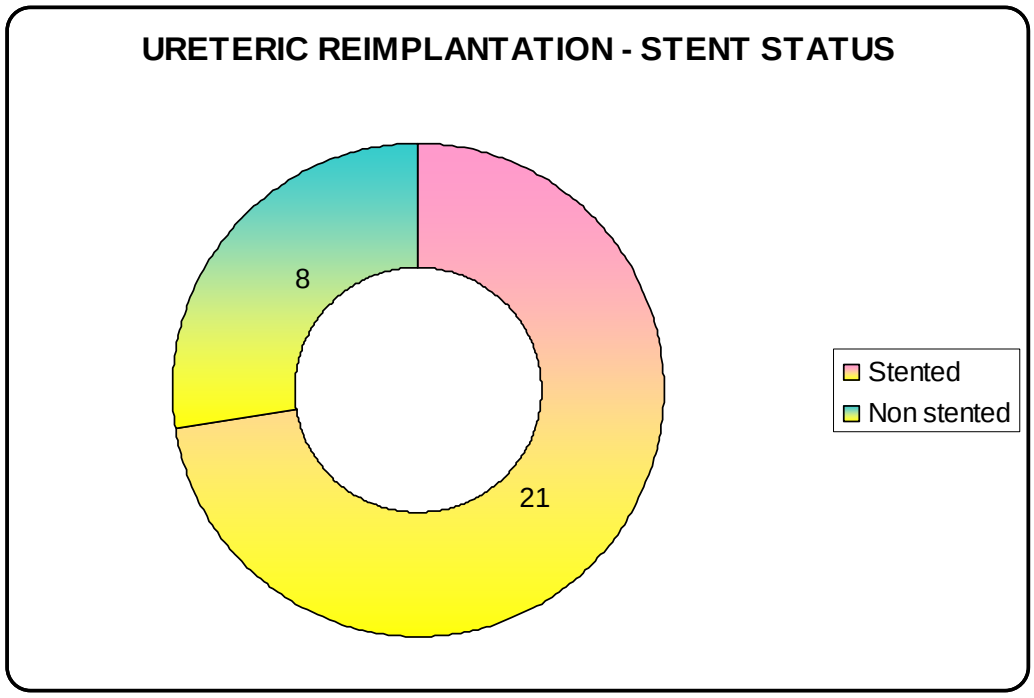
Unilateral	- Right	5 cases
	- Left	10 cases
Bilateral		14 cases
Total		29 cases

Lich Gregor & Lead better:

In one failed case with 2 renal units out of 29 cases in Cohens procedure, 1 renal unit underwent Lich Gregor and another 1 renal unit underwent Lead Better procedure.

Ureteric Reimplantation:

Stented	21 cases
Non stented	8 cases
Total	29 cases



FOLLOW UP:

All cases were followed up with a) monthly culture sensitivity for 3 months, b) USG at 3 monthly intervals for 6 months then yearly, c) MCU was done at one year post operatively.

All patients were placed on post op chemoprophylaxis for 6 months. Five patients had one episode of UTI within 6 months due to non compliance of chemoprophylaxis and they have recovered with intra venous antibiotics.

Reflux Resolution:

Total no. of renal units in our study : 56 renal units

Surgically treated : 46 renal units

Medically treated : 10 renal units

Reflux Resolution:

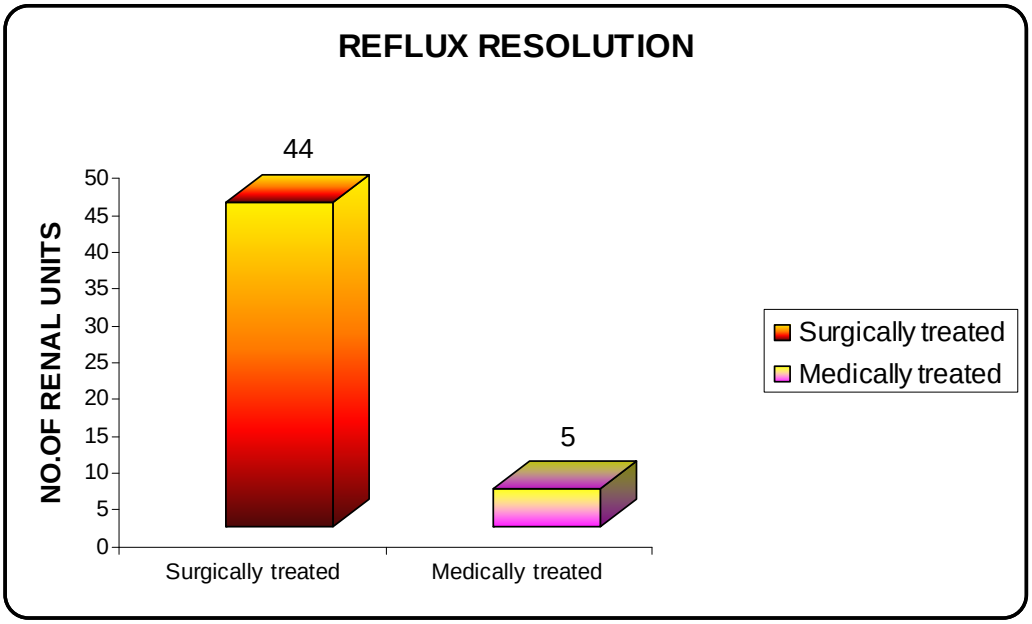
With Primary Surgery : 44 renal units

With resurgery for persistent reflux : 2 renal units*

In Medical Management 5 renal units

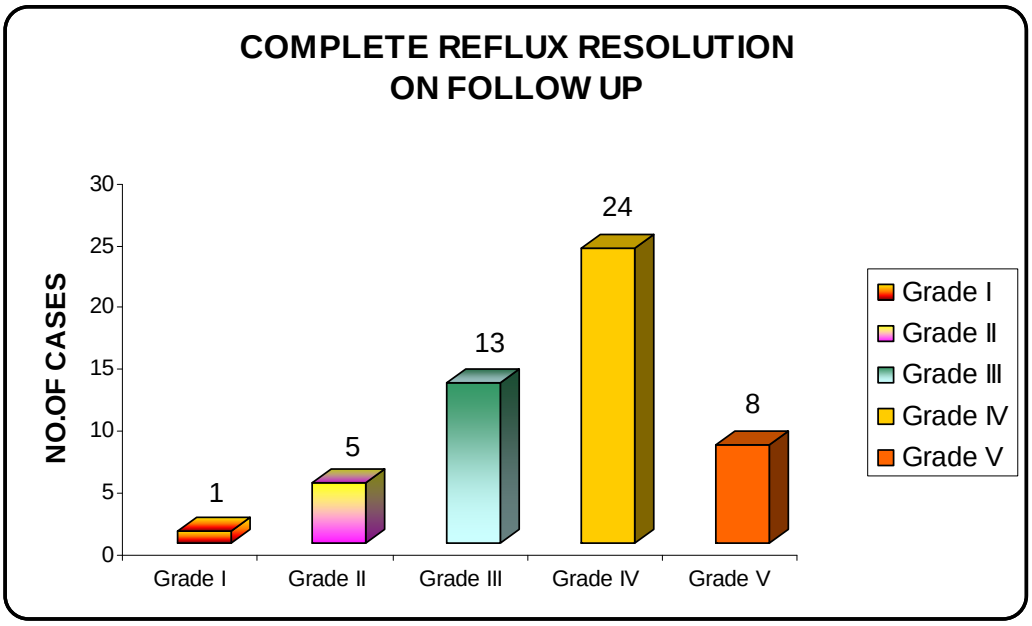
** one patients with 2 renal units with resurgery had complete resolution.*

So, 44 renal units treated by primary surgery had complete resolution of reflux.



Complete Resolution of reflux
Medical & Surgical (Primary Surgery & resurgery)

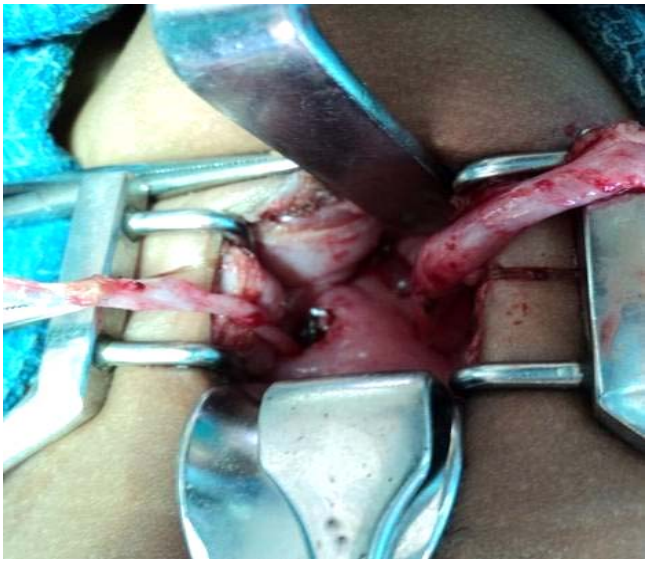
	No. of Renal Units	***Percentage***
Grade I	1	1.8%
Grade II	5	63%
Grade III	13	100%
Grade IV	24	100%
Grade V	8	80%



INTRA OPERATIVE PICTURE

CRANIAL

URETER



URETER

POST OPERATIVE MCU

Complete Resolution of reflux with initial primary surgical management is 44 out of 46 renal units with the percentage of 95.6%.

We experienced no post operative ureterovesical junction obstruction in our study, but only persistent reflux of lower grade in 2 renal units in one patient. The patient was undertaken for resurgery successfully.

The relative benefit of medical and surgical treatment of VUR, in our study is in favour of surgical management for the above observations.

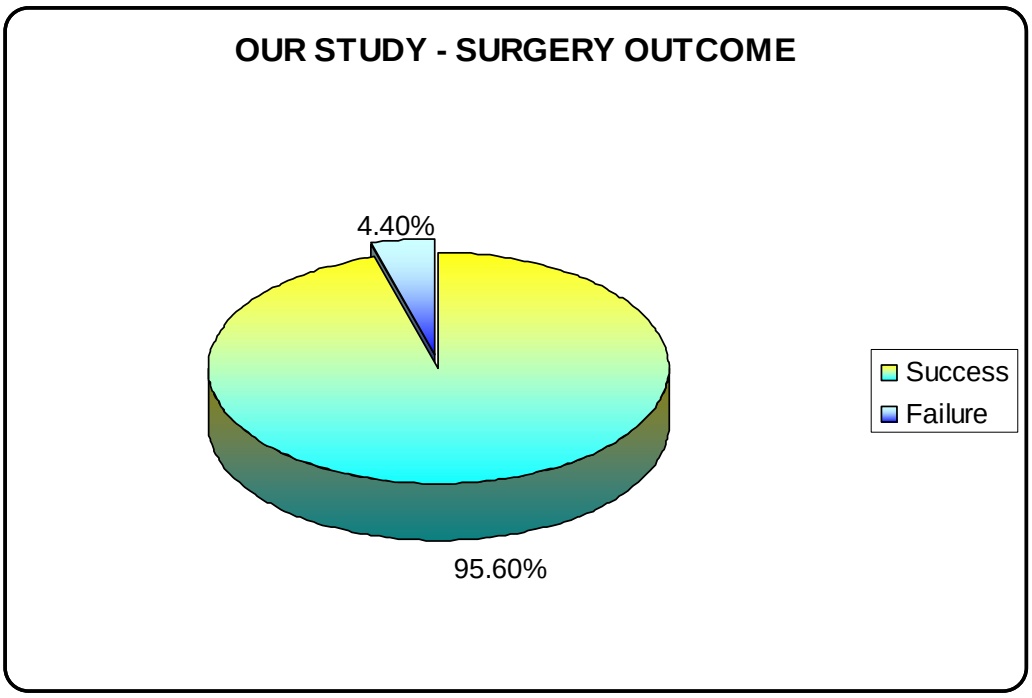
DISCUSSION

During this study period of 2½ years from August 2009 - Jan.2012, a total of 35 patients reported to the Department of Pediatric Surgery with signs and symptoms of primary vesico ureteric reflux.

In our study, 35 patients who fulfilled the criteria were taken into account and formed a total of 56 renal units. Out of these, 46 renal units were managed with surgery, 10 renal units were managed medically.

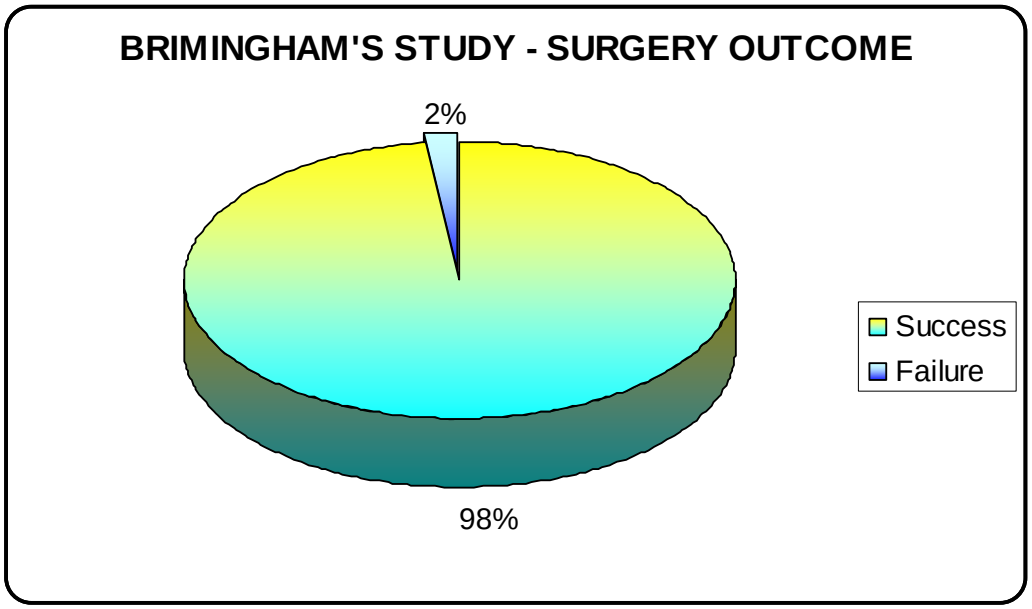
Out of these 46 renal units who had underwent primary surgery, 44 renal units got resolution of reflux with success percentage of 95.6%. The remaining 2 renal units in one patient underwent resurgery. The primary surgical technique followed in our study is Cohens Reimplant in all 46 renal units and 44 renal units had complete resolution. In the 2 failed renal units, one renal unit was managed by Lich Gregor and other renal unit was managed by Lead better.

Out of the 10 renal units who had undergone medical management, 5 got resolution of reflux with success percentage of 50%.



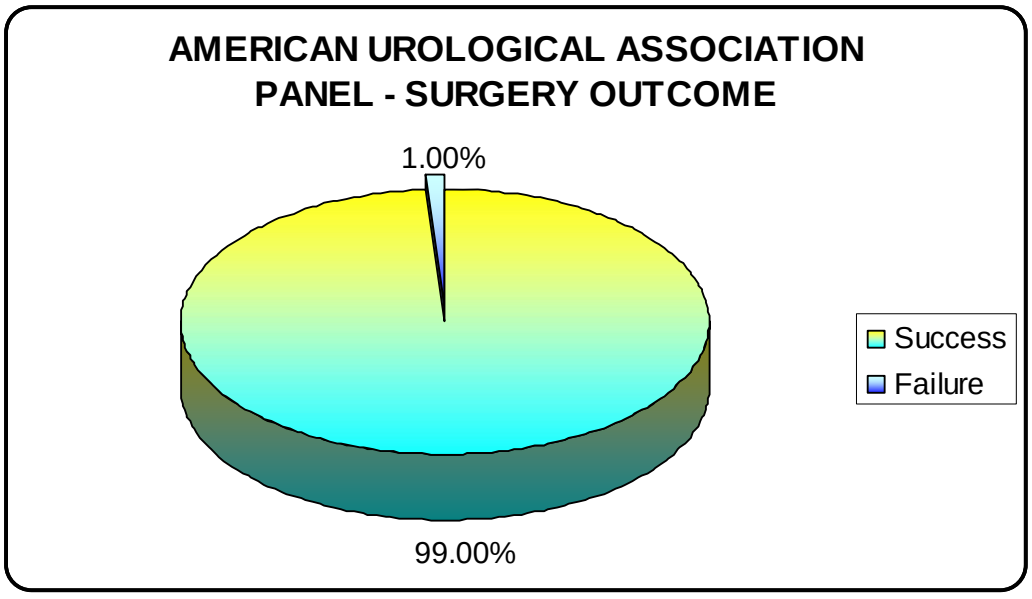
Our study results were compared with many international studies and found to be comparable.

The Brimingl rams reflux study group over a period of 5 years had 105 successful resolutions out of 107 renal units with surgical techniques of Cohen, Lich & Lead better (mainly Cohens). Success rate in this study is 98% which is comparable with our study.



In the Glassberg study over a period of 5 years, they had 100% of success rate of the 101 renal units surgically only with Cohen's technique which is very much comparable with our study.

In this American Urological Association Panel study the success rate was 99% (108/109) which is also comparable with our study.



CONCLUSION

1. Majority of cases presented at an age of <3 years and all were symptomatic with history of recurrent UTIs.

2. Male female ratio was 1:0.6, predominately males in our study.

3. Bilateral cases were 62.9% as compared to 37.1% unilateral cases.

4. Grade III, IV, V reflux constituted 83.9% of total renal units.

5. Type of surgery was predominantly Cohen's Reimplant with success rate of 95.6%.

6. In ultrasonogram, an increase in diameter of the ureter and/or renal pelvis was observed as a sign of reflux.

7. Micturiting cystourethrogram is an investigation tool for grading the reflux pre operatively and for the detection of post operative resolution.

8. Surgery is the preferred option for persistent Gr.III & IV and all Gr.V reflux.

9. Many patients who eventually required surgical management had already suffered kidney damage. So, early referral for surgical intervention would reduce the number and extent of renal damage due to reflux.

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PROFORMA – PRIMARY VUR

Name: Age: M/F

Address:

IPL No. Wt DOS

Diagnosis:

Grade: Unilateral/Bilateral Age at diagnosis:

	Pre Operative	***Post Operative***
Weight		
Blood – urea		
Creatinine		
Electrolytes		
Urine c/s		
No. of UTI		
RP		
USG – Renal size		
Ureter		
MCU		
IVU		
DTPA/DMSA		
Others		

Cystoscopy-

Type of reimplant-

Age at surgery –

Stent - Yes/No

POST op complications –

Chemoprophylaxis duration –

Follow up – age at present-

Recurrence

Symptoms

Resurgery

No. of UTI

CRF

USG – Renal size

Ureter

MCU

DTPA/DMSA

Others

MASTER CHART

S.No	Name	Age/Sex	I.P. No.	Age at Diagnosis	Rec UTI	Blood. U/C	HT	USG	MCU Grade		IVU	DMSA-scars	Pre op Chemo	Pre op Cysto-scopy	Type of Reimplant	stent	Follow up		
									R	L							MCU	Rec. UTI	Chemop-rophylaxis
1.	Dharshine	1 ½ F	704828	1yr	✓	N	–	RU 0.7cm LU 0.9cm	III	V	Faint excretion LK	Multiple B/L scars	✓	LUO-patulous RUO-difficult to visualize	B/L Cohen's	✓	Gr.II Lt. Rept. MCU N	One episode at 3 months	✓
2.	Prem	6 yrs M	515715	4yr	✓	N	–	B/L PCS prominent RK 5.5 cm LK 3.8cm	III	II	B/L prompt excretion	Upper pole B/L +ve	✓	Both UO - Normal	–	–	N	–	✓
3.	Vignesh	10 yrs M	708847	10yr	✓	N	–	LK-contr. 5.6 cm RK 8.5cm		V	LK mild UHN RK - N	B/L +ve	–	LUO patulous	Lt. Cohen's	✓	N	–	✓
4.	Arunraj	10 yrs M	703787	8yrs	✓	N	–	Rt. UHN RU 0.6cm	II	II	B/L prompt excretion	scars + dilated tortuous ureter B/L	✓	Not done	–	–	B/L Gr.II	–	✓
5.	Keerthana	10 yr F	719296	8 yrs	✓	N	–	RK Cont.	III	II	RK not visualized	Upper poles +ve LK – 85% RK – 15%	✓	RUO patulous	B/L Cohen's	✓	N	–	✓
6.	Sanjana	1 ½ yr F	718327	1 yr	✓	N	–	B/L double moiety B/L UHN RK – 8.2cm RU – 1.2cm LK – 8.9cm LU - 2.0 cm	III	IV	B/L double moiety, retention in both sides	+ve	✓	B/L golf hole ureter	B/L Cohen's common sheath reimplant, Rt. single cohen	✓	N	once	✓

S.No	Name	Age/Sex	I.P. No.	Age at Diagnosis	Rec UTI	Blood. U/C	HT	USG	MCU Grade		IVU	DMSA-scars	Pre op Chemo	Pre op Cysto-scopy	Type of Reimplant	stent	Follow up		
									R	L							MCU	Rec. UTI	Chemop-rophylaxis
7.	Kirubakaran	1 ¼ yr M	743219	*1¼ yrs*	✓	N	–	B/L HN L > R RK – 6.4cm LK – 7cm	V	IV	B/L prompt excretion	+ve	–	RUO patulous with small periureteric diverticulum	B/L Cohen's	–	N	–	✓
8.	Girthish	9/12 M	718801	9/12 months	✓	N	–	B/L UHN RK -6.5cm LK -6.8cm RU -2.4cm LU -0.7cm	IV	III	Rt. UHN draining in 6hrs, Lt. UHN hold up in 6hrs	+ve	–	RUO patulous	B/L Cohen's	✓	N	–	✓
9.	Mylarasi	2 ½ yrs F	718240	1 yr	✓	N	–	B/L UHN RK – 8.4cm LK – 7.3cm	III	II	B/L draining well	Rt. polar +ve RK – 48% LK – 52%	✓	Not done	–	–	B/L Gr.II	–	✓
10.	Jeeva	2 yrs M	713350	2yrs	✓	N	–	Lt. UHN LK – 9.4cm LU – 1.5cm		V	Lt. HN hold up in 6 hrs	RK – 94% LK – 6% +ve	–	RUO – N Lt. para ureteric diverticulum	Lt. Cohen's with diverti-culectomy	✓	N	once	✓
11.	Suresh	1 ¼ yrs M	574321	1 ¼ yrs	✓	N	–	B/L UHN RK – 6.5cm LK – 6.5cm RU - 0.6cm LU - 0.8cm		IV	drains completely in 6 hours	LK - +ve RK – 69% LK – 31%	–	normal	B/L Cohen's	–	N	–	✓
12.	Hariharan	2 yrs M	676043	1yr	✓	N	–	B/L UHN RU – 0.8cm LU – 0.4cm	IV	I	B/L bifid pelvis with polycalycosis	+ve	✓	RUO patulous	Rt. Cohen's	–	N	–	✓

S.No	Name	Age/Sex	I.P. No.	Age at Diagnosis	Rec UTI	Blood. U/C	HT	USG	MCU Grade		IVU	DMSA-scars	Pre op Chemo	Pre op Cysto-scopy	Type of Reimplant	stent	Follow up		
									R	L							MCU	Rec. UTI	Chemop-rophylaxis
13.	Ragul Kishore	4 yrs M	676106	4 yrs	✓	N	–	RK ↑ Cortical Echos RK – 8.2cm LK – 8.0cm		IV	LK delayed excretion	+ive	–	LUO close to para ureteric diverticulum	Lt. Cohen's with diverti-culectomy	✓	Lt. Gr.II Rept. MCU N	once	✓
14.	Deva dharshani	7 yrs F	491796	7 yrs	✓	Cr. mild↑	–	B/L UHN	III	III	B/L prompt excretion	+ve	–	both UO patulous	B/L Cohen's	✓	N	–	✓
15.	Surya Narayanan	2 ½ yrs M	490475	2 ½ yrs	✓	N	–	B/L UHN RK – 8.8cm LK – 9cm RU – 0.4cm LU – 0.5cm	IV	IV	B/L prompt excretion	+ve	–	Laterally placed UO B/L	B/L Cohen's	–	N	–	✓
16.	Divya	4 yrs F	684423	4 yrs	N	N	–	RK not visualized, LK HN - 6cm LU - 1.3cm			RK not visualized	No scars	–	UOs not visualized small congested bladder	Lt. Cohen's	✓	N	–	✓
17.	Bhava Saravanan	4 yrs M	606322	4 yrs	✓	N	✓	RK – 7.3cm LK - small 5.9cm		IV	Lt. UHN	Lt. polar +ve	–	LUO patulous	Lt. Cohen's	–	N	–	✓
18.	Keerthika	3 yrs F	677564	3 yrs	✓	N	–	B/L UHN RK – 6.9cm LK – 7.1cm RU - 0.8cm LU - 0.6cm	IV	IV	LK delayed excretion	multiple B/L +ve RK – 63% LK – 37%	–	normal	B/L Cohen's	–	N	–	✓
19.	Kavya	1 yr F	720634	6 months	✓	N	–	Rt. UHN RK – 6.7cm LK – 6.2cm RU – 0.4cm LK – 0.8cm	IV		–	Multiple B/L +ve	✓	Both UOs visualized	Rt. Cohen's	✓	N	–	✓

S.No	Name	Age/Sex	I.P. No.	Age at Diagnosis	Rec UTI	Blood. U/C	HT	USG	MCU Grade		IVU	DMSA-scars	Pre op Chemo	Pre op Cysto-scopy	Type of Reimplant	stent	Follow up		
									R	L							MCU	Rec. UTI	Chemop-rophylaxis
20.	Vignesh	9 yrs M	727561	7 yrs	✓	N	–	LK - PCS dilatation LK – 6.2cm RK – 9.0cm Lt. lower ureter seen		III	Lt. Sec. PUJO	Rt. upper pole +ve RK – 92% LK – 8%	✓	RUO – N LUO larger	Lt. Cohen's	✓	N	–	✓
21.	Thasmin banu	2 yrs F	742600	2yrs	✓	N	–	RU – 0.9cm LU – 0.9cm	IV	IV	draining completely in 6 hrs	multiple B/L +ve RK – 50% LK – 50%	–	BUO patulous Laterally placed	B/L Cohen's	–	N	–	✓
22.	Naresh kumar	10 yrs M	743312	10 yrs	✓	N	–	B/L UHN RK – 7.8cm LK – 7.6cm RU – 0.7cm LU – 0.3cm	III		draining completely in 4 hrs	multiple B/L +ve RK – 21% LK – 79%	–	RUO laterally placed	Rt. Cohen's	✓	N	–	✓
23.	Sharmila	6 yrs F	651055	6yrs	✓	N	–	RK – 8.2 cm LK – 4.6cm LU 1.1cm		III	LK delayed excretion	LK Cortical +ve RK – 75% LK – 25%	–	Not done	–	–	N	–	✓
24.	Rena Juliet	4 yrs F	559259	4 yrs	✓	↑	–	Rt. UHN double moiety	V		RK not visualized	RK +ve RK – 15% LK – 85%	–	Ruo patulous	Lead better politano Rt.	✓	Gr.II Rept. MCU N.	once	✓
25.	Ashok	3 yrs M	663791	3 yrs	✓	N	–	B/L mild pcs dilatation RK – 4.3cm LK – 8.1cm RU – 0.7cm	III	III	B/L prompt excretion	RK +ve RK - 15% LK - 85%	–	BUO patulous	B/L Cohen's	✓	N	–	✓

S.No	Name	Age/Sex	I.P. No.	Age at Diagnosis	Rec UTI	Blood. U/C	HT	USG	MCU Grade		IVU	DMSA-scars	Pre op Chemo	Pre op Cysto-scopy	Type of Reimplant	stent	Follow up		
									R	L							MCU	Rec. UTI	Chemop-rophylaxis
26.	Devendran	5 yrs M	622123	3yrs	✓	N	–	B/L UHN	II	V	B/L prompt excretion	LK Cortical +ve	✓	Normal	B/L Cohen's	✓	N	–	✓
27.	Rahul Kumar	7 yrs M	590429	7 yrs	✓	N	–	B/L UHN		V	B/L prompt excretion	B/L +ve	–	Normal	Lt. Cohen's	–	N	–	✓
28.	Vinoth	2 yrs M	538166	*2 yrs*	✓	N	–	Rt. UHN Lt. MCDK	IV		LK not visualized	RK +ve	–	LUO not visualized	Rt. Cohen's	✓	N	–	✓
29.	Vignesh	3 ¼ yrs M	521414	*3 MONTHS*	✓	↑	–	RU – 2.1cm LU -1.2cm	IV	IV	–	RK – 74% LK – 26%	–	BUO patulous	Lt. Cohen's repeat Lt. lich gregeor, Rt. Cohen's	✓	B/L VUR Re-surgery then MCU N	once	✓
30.	Karthigayan	2 ¼ yrs F	677564	2 ¼ yrs	✓	N	–	B/L UHN RU - 0.6cm LU - 0.6cm	IV	IV	draining completely in 6 hrs	B/L cold areas present RK – 63% LK – 37%	–	BUO patulous laterally placed	B/L Cohen's	✓	N	–	✓
31.	Asen Goswa	3 yrs M	642084	6 months	✓	N	–	RK – 4.8cm cor.thickness 0.5cm LK – 8.5cm Normal Cortex	IV	III	RK delayed excretion	RK – 17% LK – 83% +ve	✓	LUO patulous	Lt. Cohen's	✓	N	–	✓
32.	Satheeswari	1 ¼ yrs F	653513	1 ¼ yrs	–	N	–	B/L UHN	III	III	draining completely in 6 hrs	Polar B/L +ve RK – 45% LK – 55%	–	Not done	–	–	Lt. Gr.II	–	✓

S.No	Name	Age/Sex	I.P. No.	Age at Diagnosis	Rec UTI	Blood. U/C	HT	USG	MCU Grade		IVU	DMSA-scars	Pre op Chemo	Pre op Cysto-scopy	Type of Reimplant	stent	Follow up		
									R	L							MCU	Rec. UTI	Chemop-rophylaxis
33.	Vijayakumar	3 yrs M	648798	3 yrs	✓	N	–	B/L UHN Lt. > Rt. RU – 0.3cm LU – 1.1cm	IV	V	LK delayed excretion	Not done	–	B/L golf hole UOs	B/L Cohen's	✓	N	–	✓
34.	Srinivasan	2 ½ yrs M	648657	2 ½ yrs	✓	N	–	B/L UHN RK – 10.7cm LK – 10.5cm RU – 1.1cm LU – 1.2cm	IV	V	B/L prompt excretion	Not done	–	B/L para ureteric diverticulum	B/L Cohen's	✓	N	–	✓
35.	B/o. Valli	14 days M	651085	*AN diag B/L UHN*	-	N	–	B/L UHN RU – 0.6cm LU – 0.8cm	II	IV	-	Not done	✓	-	–	–	Lost to follow up		

PATIENT INFORMATION SHEET

AIM OF THE STUDY

In primary vesicoureteric reflux this study is to do analysis of post surgical outcome in Primary vesicoureteric reflux; a 3 year study among the children admitted in Institute of Child Health, Egmore, Chennai a tertiary referral hospital and also a premier state apex pediatric institute.

All data will be kept strictly private and confidential. You may choose to take part or not in this study. That is your choice. No penalties or loss of benefits will come from refusing. Even if you have choosen to take part, you may refuse to answer any question. Even if you do not take part in this study, as per the treatment protocol the treatment strategies will be the same.

If you have any doubts regarding this study, you can meet the investigator to get them clarified. In this study all investigations are done at free of cost. The treatment given is also free of cost.

SECTION – II
INFORMATION CONSENT FORM

I agree to participate in the study titled Primary vesicoureteric reflux an analysis of Post surgical outcome in primary vesicoureteric reflux.

I confirm that I have been told about this study in my mother tongue and I had the opportunity to ask question. I confirm that I have been told about risk and potential benefits for my child participation.

I understand that my child participation is voluntary and I may refuse to continue at any time without giving any reason without my child's benefits being affected.

1. Name of the Child
2. Name of the Guardian/Care Giver :

   Signature :

   Date :
3. Name of the Witness :

   Signature :

   Date :
4. Name of the Investigator :

   Signature :

   Date :

பகுதி – 1
தகவல் தாள்

ஆய்வின் நோக்கம்

நமது சென்னை எக்மோர் குழந்தைள் மருத்துவமனையில் – (உயர்வான, மூன்றாம் நிலை பரிந்துரைப்பு மருத்துவமனை) குழந்தைகள், **Primary Vesico Ureteric Reflux** நோயிற்காக அறுவை சிகிச்சை – செய்த பின், எவ்வாறு உள்ளனர் என்பதை ஆராய்வதே இந்த ஆய்வின் நோக்கம்.

ஆய்வில் வழங்கப்பட்ட மற்றும் சேகரிக்கப்பட்ட விவரம் இரகசியமாக பாதுகாக்கப்படும். இந்த ஆய்வில் தங்கள் குழந்தை பங்கேற்பது உங்களது விருப்பத்தைப் பொறுத்து. இந்த ஆய்வில் சேரமால் இருப்பதால், மருத்துவ சிகிச்சை அளிப்பதில் எந்வித இடர்பாடும் நேராது. ஆய்வில் பங்கேற்கும்போது இடையில் ஷிலகவோ, கேள்விகளுக்கு விடையளிக்காமல் இருக்கவோ தங்களுக்கு உரிமை உள்ளது. மேலும் இந்த ஆய்வில் சேராவிட்டாலும், இந்த நோய்க்கு அறுவை சிகிச்சைதான் ஒரே வழி என்பதையும் அறிந்துகொண்டேன்.

ஆய்வு குறித்து தங்களுக்கு ஏதேனும் சந்தேகம் ஏற்பட்டால் ஆய்வாளரை நேரில் சந்திக்கவோ, தொலைபேசியில் தொடர்பு கொள்ளவோ வரவேற்கப்படுகிறீர்கள்.

அபாயங்கள் மற்றும் நன்மைகள்:

இந்த ஆய்வில் பங்கேற்பதால் எந்வித தீங்கும் ஏற்பட வாய்ப்பில்லை. இதில் பங்கேற்கும்போது செய்யப்படும் மருத்துவ பரிசோதனைகள் மற்றும் சிகிச்சை முறைகள் முற்றிலும் இலவசமானது.

பகுதி – 1
ஒப்புதல் படிவம்

1. நான் இந்த _____ தேதியிட்ட தகவல் தாள் படிவத்தை நன்றாகப் படித்து / படித்துக் காட்டி எடுத்துரைத்ததை புரிந்து கொண்டேன். எனக்கு கேள்வி கேட்கும் வாய்ப்பும் கிடைத்தது.

2. இந்த ஆய்வில் நான் என்னுடைய சுய சிந்தனையோடு பங்கு கொள்கிறேன். மேலும், இந்த ஆய்விலிருந்து எந்த விதக் காரணமும் தராமல் மருத்துவப் பரிசோதனையிலிருந்து நான் விலகிக் கொள்ளலாம். இதனால் சட்டரீதியான எந்த செயலும் என்னை உட்படுத்தாது.

3. Ethics குழுவின் அங்கத்தினர்களோ, இந்த ஆய்வை நடத்துபவர்களோ என்னுடைய மருத்துவ ஆய்வின் அனைத்து விவரங்களையும் என்னுடைய அனுமதியின்றி பார்க்கவோ, படிக்கவோ உரிமையுள்ளவர்களாவர். நான் இந்த ஆய்விலிருந்து விலகிக் கொண்டாலும்கூட என்னுடைய விவரங்களை அவர்கள் அறிந்து கொள்ள ஒத்துக் கொள்கிறேன். என்னுடைய விவரங்கள் அனைத்தும் 3வது நபருக்கோ, அல்லது பத்திரிக்கையில் வெளியிடுவதற்கோ முயலமாட்டீர்கள் என நம்புகிறேன்.

4. இந்த ஆய்விலிருந்து பெறப்பட்ட புள்ளி விவரங்களையோ அல்லது முடிவுகளையோ பயன்படுத்த கூடாது என்று கட்டுப்படுத்த மாட்டேன்.

5. இத்தொடராய்வில் செய்யப்படுகின்ற செய்முறைகளினால் ஏற்படும் பக்க விளைவுகளுக்கு மருத்துவ உதவி செய்யப்படும். எந்தவித நஷ்ட ஈடும் தரப்படமாட்டாது என்பதையும் அறிந்து கொண்டேன்.

6. என் குழந்தையை இந்த மருத்துவ ஆய்விற்கு பங்கு கொள்ள பரிபூரணமாக சம்மதிக்கிறேன்.

கையொப்பம்: தேதி: Signature of the Investigator

பெயர்: Signature of witness:

குழந்தையின் பெயர்: